EXHIBIT 1

UNITED STATES DISTRICT COURT

DISTRICT OF NEW JERSEY

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IN RE: PROTON-PUMP INHIBITOR PRODUCTS LIABILITY LITIGATION

2:17-MD-2789(CCC)(MF)

(MDL 2789)

Judge Claire C. Cecchi

This Document Relates to:

All Actions

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REMOTE HEARING

BEFORE SPECIAL MASTER ELLEN REISMAN

Monday, April 4, 2022

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This is the Remote Hearing In Re: Proton-Pump Inhibitor Products Liability Litigation, commencing at 10:00 a.m., Monday, April 4, 2022, before Juliana F. Zajicek, Registered Professional Reporter, Certified Shorthand Reporter and Certified Realtime Reporter.

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THE SPECIAL MASTER: All right. So let's go on the record. And so what we are doing today is oral argument on the various Daubert motions and on our defense motions for summary judgment. And a couple of things I just wanted to say upfront.

I looked at the outline that we did, the procedures outline, and I think we left out the Mann -- Mann's name on -- on the oral argument on plaintiffs' omnibus motion to exclude experts. I think it should have been on there.

I also noted that it looks to me like we are having argument on four plaintiff experts and five defense experts and I -- you know, the timeframes are a little bit longer as to the plaintiffs' experts, shorter as to the defense experts. I'm obviously, you know, if need be will allow people to have some additional time, although I'm really hoping that we don't end up using all of the time. I think, as I was sitting down and calculating this this morning, it is a lot of time, and believe it or not I have actually read all of this stuff. There are many large notebooks strewn around this room, and because I -- I have to read things in hard copy. So we killed a lot of trees here.

I would appreciate, and I think we said this in the procedures, if there are particular points that you think might be unappreciated from the -- the papers, that you emphasize those, but other -- otherwise, you know, I don't -- you don't need to rehash everything that's in the papers because I've read them and my partner Andy has read them, and so, you know, I think -- I think maybe we could not spend all day together, as delightful as I'm sure that will be.

One thing -- one thing I wanted to raise just in the way of full disclosures upfront, there is -- I don't know any of these experts personally except one who I did meet years ago, somewhere between 15 and 20 years ago, and that's Mary Ann Mann, and I think I had one meeting with her in connection with a case I was working on at the time. Not surprising, I've been doing this for 37 years. Honestly, I would have thought more of them might have crossed my path, but -- but I just wanted people to know that in the interest of full disclosure.

So with that, let's get started and somebody should raise their hand, whoever is going to address the motion.

I think Wells is the first one?

Okay.

MS. DU PONT: Good morning, Special Master. My name is Julie du Pont. I'm going to be speaking on behalf of AstraZeneca.

And if I have your permission, do you mind if I share some slides to assist with my argument?

THE SPECIAL MASTER: Sorry, I'm not the most technologically sophisticated. Yes, it is fine for you to share some slides. Okay.

MS. DU PONT: Can you see those?

THE SPECIAL MASTER: Yes, I can.

MS. DU PONT: Good morning, Special Master. Defendants' brief on Dr. Wells, I think, clearly sets forth the defendants' argument as to why Dr. Wells should be excluded under Daubert, and consistent with what the Special Master just said, I'm not going to belabor and repeat all of those arguments that were set forth in our motions. I think my point today is simply to briefly underscore a few key issues for the Special Master. And that's what I will be doing.

First, the central issue in both Rieder and in Bales that the jury will need to decide is whether PPIs caused each of these plaintiffs' chronic

kidney disease. Tellingly here, we know that Dr. Wells is not offering an opinion about whether PPIs cause chronic kidney disease.

At his deposition he was asked:

"...are you offering an opinion that -- that your calculation and the change in eGFR establishes to a reasonable degree of medical certainty that PPI use can cause kidney injury?"

His answer: "No."

And plaintiffs acknowledge in their motion that they are not offering causation -- that he is not offering causation opinions with respect to PPIs and CKD.

They likewise state --

THE SPECIAL MASTER: Can I ask you a question, can I interrupt and ask you a question?

MS. DU PONT: Sure.

THE SPECIAL MASTER: Are you saying that any expert who says they are not offering causation opinions should be excluded?

MS. DU PONT: No, that's not what I'm saying. What I'm saying is that Dr. Wells' testimony needs to provide -- needs to be relevant to the issue and the issues in this case, and I will add that not only is

he not offering causation opinions, he admits he is not doing any hypothesis testing and that he admits that his opinions don't offer any clinical significance.

THE SPECIAL MASTER: But aren't there a lot of -- I mean, there are other experts, I mean, I've been through all of them now, who are -- who are offering opinions that do not reach the ultimate conclusion of whether a PPI product caused the plaintiff's CKD and they are still providing relevant and admissible evidence, I believe.

So I'm not -- I'm not sure why that would be an -- especially given his field, he is a biostatistician, and they often don't provide causation evidence, they just tell you about the data.

MS. DU PONT: Well, Dr. Wells has in other cases provided causation testimony before, but as you can see, he has not offered that here. And not only is he not offering any causation testimony, as I just mentioned, he is -- he is not even testing any relevant hypothesis through his metaanalysis, including the -- the particular hypothesis that PRAC looked at, and that was plaintiffs' argument, was that he was offering some sort of rebuttal to PRAC's --

PRAC's opinion, but, in fact, he repeatedly admitted that he wasn't doing any hypothesis testing whatsoever, and that he had no knowledge of what PRAC really does generally or specifically did with respect to PPIs here.

So not only is he not offering causation opinion, he doesn't provide any fit to the relevant issues in this case whatsoever.

THE SPECIAL MASTER: Well, one question I had, in the plaintiffs' papers, I think they said that the analyses that he is performing were ones that had been requested by PRAC and not done by AZ, is that correct?

MS. DU PONT: I don't believe that is correct.

What -- what Dr. Wells did was he first conducted the meta-analysis doing what essentially AZ did and PRAC reviewed, which was including the four-week studies. He then did an analysis where he excluded those less than four-week studies, and finally got the opinion that he wanted, that there was a decline in eGFR.

THE SPECIAL MASTER: And so are you saying that there was no legitimate scientific basis for him to exclude -- to exclude the four-week studies and that's -- and is that the basis -- I know in your

papers you say that his methodology was result driven.

Is that the basis for why you say it was result driven?

MS. DU PONT: I mean, I think that -- that Dr. Wells offers the explanation that he spoke with some of the plaintiffs' expert nephrologists and they believed that the four-week studies -- the less than four-week studies, I should say, would not add anything, but that is at odds with what PRAC itself said, first of all. And the fact of the matter is the way in which Dr. Wells conducted his analysis suggests it was with -- it was results driven. And what I mean by that is he -- he says -- he puts in his report only the metaanalysis where he excludes the four-week data.

When asked after the fact at his deposition whether he had conducted analyses including the four-week data, he explained that he actually did that analyses first and that then didn't find a significant decline in kidney function with that analysis. So he did the second analysis excluding those studies and actually found a decline in kidney function.

What is bothersome about that approach is if you thought he was going to conduct the

metaanalysis with his -- the intent to exclude those four-week studies, shouldn't he have done that first and then pressure test it by adding them back in? He did not do so. So his after-the-fact explanation sort of defies common sense.

If it is okay, Special Master, I can move on to our second argument in the brief?

THE SPECIAL MASTER: Yes, go right ahead. Thank you.

MS. DU PONT: And here, and I'll just stop sharing my screen, I just want to emphasize the two courts that have recently excluded Dr. Wells for similar results driven meta-analyses. The first is the In Re Incretin case in the Southern District of California decided just last year, where the court found that he had no adequate scientific reason for his metaanalyses, that his method was arbitrary and not scientifically sound. The second case is In Re Byetta, California Supreme -- Superior Court, also decided last year, again, the court found no scientifically reliable basis for Wells' litigation decision-making where he arbitrarily changed his analysis by excluding certain data from his metaanalysis and got a different result.

Here we know that Dr. Wells arbitrarily excluded several four-week studies after first conducting an analysis that included them. It was only after excluding those studies that he got the significant decline in kidney function. He then only presented that second analysis in his report.

The Special Master should follow the reasoning of In Re Incretin and In Re Byetta and similarly exclude Dr. Wells' opinions here.

And I'll reserve the rest of my time.

Sorry. Do you have another question?

THE SPECIAL MASTER: Okay. Yeah. I assume that you expect to be offering the PRAC data at trial, is that right?

MS. DU PONT: That -- that is not necessarily true. I think the part -- that AstraZeneca intends to move to exclude foreign regulatory. Now, whether or not we win that motion is a -- is a decision yet to be decided, but, no, I would not assume that we will be relying on PRAC at trial.

THE SPECIAL MASTER: I don't think I have any other questions for you. Thank you.

MS. DU PONT: Thank you.

THE SPECIAL MASTER: Who is up next?

Okay, James.

MR. MIZGALA: Good morning, Special Master. I just want to just emphasize a point about PRAC. Takeda did not put PRAC in their preemption and we did our own analysis, our epidemiologist has done his own analysis of the clinical trial data. So we won't be offering the PRAC data, but even if we were, the fact is, is that Wells can't tell you what his analysis mean in terms of the safety of PPIs and no other expert on plaintiffs' side has taken his analysis and said, This is what it means. So what's a jury supposed to do with that when he can't even tell you what the clinical significance of his data is. And I'll reserve the rest of my time unless you have a question.

THE SPECIAL MASTER: Okay. Thanks, Jim.

Who from plaintiffs' side is going to be responding?

Stephanie. Hi.

MS. O'CONNOR: Hi, Ellen. Hi.

THE SPECIAL MASTER: Okay.

MS. O'CONNOR: Stephanie O'Connor for the plaintiffs. And I will be arguing in opposition to both AstraZeneca and Takeda's joint motion, as I

understand it to preclude or exclude Dr. Wells.

First of all, let me say that all Dr. Wells did was take the same data that -- with regard to AstraZeneca, that AstraZeneca produced to PRAC and conducted a metaanalysis that the PRAC actually asked about in the incident of signal CKD detection back in September of 2016. They asked to receive data on all clinical trials that had looked at kidney function data, gave as examples estimated glomerular filtration, or GFR, and asked for a metaanalysis if available.

Now, what the companies did was they provided essentially summary arithmetic measures, summary statistics. They didn't provide individual patient-level data. They provided summaries across studies.

In the case of AstraZeneca, who has conducted over 1600 studies, perhaps even 2,000 studies, up to that number, they submitted 22 studies in response to Question No. 3 from PRAC seeking information on kidney function.

Takeda has conducted hundreds of studies across the three products that they submitted data for, that being lansoprazole, dexlansoprazole, and

pantoprazole, submitted a total of seven studies. All right.

So to the extent that we hear that there was cherry-picking or selection of studies, it is the defendants actually who have engaged in cherry-picking and selective process in providing information to the PRAC.

And the reason it is relevant, not having to do with whether or not PRAC is a foreign regulatory agency, but they cannot use it as both a shield and a sword. They can't say that Dr. Wells can't talk about his statistical interpretation of the same data that was submitted to the regulatory authorities in Europe and yet hold that data up, including in communications with the FDA, to say that the clinical trial data is clean.

In the preemption motion they do talk about the significance of the clinical trial data. I heard your question and answer from Ms. DuPont, and as we sit here today, we don't know what the answer is to that. But Dr. Wells should be able to and the plaintiffs should be able to rebut claims by the manufacturer defendants that their clinical trial data is clean and that there is no problem.

We've heard it throughout this litigation. It started on science day and it has continued through the depositions of practically every expert that I have defended in this case.

THE SPECIAL MASTER: Can I -- can I ask you a question, Stephanie?

So they've made the point that, you know, he is not going to talk about, you know, whether PPI's cause CKD in a particular case or more generally and -- and that I think Mr. Mizgala made a comment that he wouldn't be able to tell what the safety data -- what the data mean for safety purposes.

What exactly is the testimony that you envision this witness offering and how is that relevant to the case.

MS. O'CONNOR: So basically, as we know, and you pointed out in your questioning, Dr. Wells is not a medical doctor. He has conducted a biostatistical analysis, as biostatisticians do, on data, again, submitted by both the manufacturers to PRAC in support of their claim that there is nothing in the clinical trials to be concerned about.

By the time Dr. Wells would testify at trial, we will likely have heard from at least two

nephrologists, board certified nephrologists, and the jury will have learned through the course of the plaintiffs' case what estimated glomerular filtration rate means, or eGFR. And we all know, sitting here, that a reduction in eGFR is associated with renal disease, all right, a reduction of, I believe it is less than 60 milliliters per minute squared for a period of greater than three months.

By the time Dr. Wells gets on the stand, the jury will know what GFR is and he would present the forest plots that are attached as Exhibit A to show where it is the reductions are seen. It is a statistical analysis.

He will explain that everything to the left of 1 as seen in every one of the forest plots for both AZ and for Takeda shows a statistically significant reduction in glomerular filtration rate.

Now, he is not going to, as a nonmedical person, testify about the significance of that. That will be left to the plaintiffs' nephrology experts of whom two have been designated in Mr. Rieder's case.

THE SPECIAL MASTER: I thought I heard one of the -- either Julie or James say that none of the other experts are going to rely on his testimony, his

data.

Is that -- is that correct?

MS. O'CONNOR: I think it is a misstatement of the situation. All of the experts had Dr. Wells' report on their materials considered list.

Dr. Ross discusses, because his report was due about a month later, discusses in detail at Pages, I believe it's 363 and 364 of his report, discusses in detail the Wells' metaanalysis, pointing out that while the defendants could have done it, they didn't, and Dr. Wells did the very type of statistically sound, methodologically sound metaanalysis of their clinical trial data.

The experts have reviewed Dr. Wells' data, they didn't dispute the data, they formed their own opinions, of course, as experts must and do, but they did consider Dr. Wells' analysis.

THE SPECIAL MASTER: Okay. Before we run out of time, I wanted to ask about those two cases where he was excluded. And I don't remember which was which, but one of them did involve, I think, one of the same criticisms the defendants are making here, which is that data were arbitrarily excluded from -- from an analysis and, you know, it seems -- we looked at those

cases as well, and it seems somewhat analogous, frankly, to the facts here.

Do you have any response to that?

MS. O'CONNOR: Yes, I do.

First of all, both of the decisions that they cite to concern Byetta, also known as incretin or vice versa. The first of those two cases, which is the incretin decision, came out in March of 2021 followed within a month by the Byetta decision. The incretin decision is a District Court of California trial court, and the Byetta decision, again, it's the same product or -- same product, is the State Court in California.

So first and foremost, neither of these are Circuit Court cases, appellate-level cases.

I think that there is a difference, if you read -- essentially they are saying the same thing, both the State Court and the -- and the Federal Court.

First and foremost, the claim that there was no scientific basis for the exclusion of the studies that Dr. Wells excluded in that case, all right. Here we have a much, much different situation. As Dr. Wells described, all right, he did three -- basically three things.

First, he reviewed the Signal Assessment report by the rapporteur as well as comments by the member states. That is attached as an exhibit to -- Exhibit 4 to the Wells opposition.

And what I'd like to do, Ellen, if I may, since I think I do have some time left, is read from Page 13 of 26 of Exhibit 4, which is an assessor's comment in a dialogue box in which they are looking at the Takeda data, which is the 12-week or more studies in terms of the duration. And they note that there is a difference, that they submitted studies no less than 12 weeks of duration, and the statement, and I read from that document in the dialogue box:

"It is reasonable to suppose that shorter trials would tend to be less likely to detect events of interest or evidence of changes in kidney function than longer trials because of their shorter duration. It is unlikely that excluding such trials would bias the results of the analysis away from detecting an association between lansoprazole and CKD or kidney dysfunction."

Obviously it includes by definition the four-week studies, the shorter duration studies that Dr. Wells ultimately excluded from his analysis in

arriving at his opinions.

So he saw this information, then he saw that Takeda itself, in submitting its data and its response to the PRAC, indicated that it was relying upon the KDIGO definition of CKD, which I mentioned earlier, that being a GFR less than 60 milliliters per minute squared for a period of greater than three months. By definition, the four-week studies have no relevance.

And finally, the third thing that Dr. Wells did as distinguished from what occurred in the Byetta and the incretin cases is he consulted with two nephrologists who told him, and he disclosed it, they had the opportunity to ask him about it, they asked very little, but they told him that the four-week studies were unlikely to yield any change in GFR that would inform a nephrologist or anyone looking at data like this as to whether there really was a change in renal function.

THE SPECIAL MASTER: Okay. Thanks, Stephanie. I think your time is up, but thank you.

Julie or James, do you want to respond?

MS. DU PONT: I would like to respond, if that's okay.

THE SPECIAL MASTER: Yes, go ahead.

MS. DU PONT: I first just want to point out that Dr. Ross was specifically asked at his deposition whether he was relying on Dr. Wells' analysis and he specifically answered no.

Plaintiffs seem to suggest that Dr. Wells is offering a rebuttal opinion about the kind of analysis that the defendant should have submitted to PRAC, but Dr. Wells has repeatedly admitted that he is not doing any sort of hypothesis testing, including whether he was testing the hypothesis that PRAC was looking at. And, in fact, he has admitted that he doesn't have specific knowledge about what PRAC actually did here or general knowledge about what PRAC does generally.

I'd also add that the preemption issue is a legal issue for the court to decide and does not provide a basis for Dr. Wells to offer any opinions to the jury. The Supreme Court held in Albrecht that:

"We here decide that a judge, not the jury, must decide the preemption question.

"In those contexts where we have determined that the question is 'for the judge and not the jury,' we have also held that 'courts may have to

resolve subsidiary factual disputes' that are part and parcel of the broader legal question."

Simply put, the jury will not be addressing preemption and so what Dr. Wells said about PRAC has no relevance here.

And then, finally, just -- just with respect to -- I'll -- I'll stop there. Thank you.

THE SPECIAL MASTER: Okay. James?

MR. MIZGALA: Just quickly.

Ms. O'Connor mentioned that Wells is going to get up and talk about his analysis and then the jury is going to hear that and somehow the jury is going to know what the clinical significance of an -- of his findings are, because these nephrologists, which she didn't name, but the two at issue are Fine and Powers, and I'm looking at Dr. Powers' deposition transcript, and he says that Dr. Wells' report is not one that he had reviewed in connection with this case.

So there -- those opinions have never been disclosed, that any one -- any one of their experts has relied on Dr. Wells' analysis. It is not in their response. You'll notice there is a footnote that starts going down that road, but it is incomplete, and so they can't point to any affirmative evidence that

any of their experts have relied on Dr. Wells' analysis.

What they want to do is throw it out there and let the jury speculate as to what it means, and that's -- that's just not right.

THE SPECIAL MASTER: Okay. Thanks.

MS. O'CONNOR: Ellen, I'm sorry, may I just address one thing?

THE SPECIAL MASTER: Sure.

MS. O'CONNOR: Please allow me. Thank you. I appreciate it.

With respect to -- I'll just address AZ's argument, I think I've already said what it is that we would prepare, how we would present Dr. Wells. I've heard more than once and I've seen in the papers this business about hypothesis testing.

Dr. Wells -- first of all, the EMA didn't ask for hypothesis testing. They asked for a metaanalysis and a metaanalysis includes significance testing, the calculation of confidence intervals. That is something that neither AZ or Takeda did, but Dr. Wells did it.

And why did he do it? Because you just can't, to use an analogy, have a jigsaw puzzle with a

thousand pieces, put it on the table and say here it is. What you have to do is you've got to connect the dots, you've got to put the pieces together, present the picture and show what it means. And you do it in a statistical interpretation and analysis by doing calculations of confidence intervals by doing significance testing, none of which was done by either of the defendants in this case.

THE SPECIAL MASTER: Okay. Thank you.

All right. Let's move on to Gilbert Moeckel, and I think there are two motions pending with regard to him. One is the qualification motion and one is a motion to exclude his testimony.

And who is going to argue that one?

Okay. Katherine, go ahead.

MS. ALTHOFF: Hi, good morning, Special Master. My name is Katherine Althoff. I don't think we've met before. So I am pleased to meet you today.

THE SPECIAL MASTER: Nice to meet you.

MS. ALTHOFF: Nice to meet you. I am representing AstraZeneca on these motions and my colleague James Mizgala from Takeda is also going to be, I think, speaking on these motions as well.

As you saw, the motion to disqualify

really relates to AstraZeneca, but the motion to exclude addresses both defendants. So I actually have a few slides that I'm going to share as well here.

THE SPECIAL MASTER: I'd like to start with the --

MS. ALTHOFF: Sure.

THE SPECIAL MASTER: -- the motions to disqualify, if we can, because I think, you know, that obviously is -- is -- well, I'd just like to start with that one.

MS. ALTHOFF: I agree, because if the -- you know, if he is disqualified then in fact there is not much to talk about on a motion to exclude. So I think you should -- do you have it in front of you, can you see it?

THE SPECIAL MASTER: Yes, we see it.

MS. ALTHOFF: Okay. Great.

So, your Honor, again, with regard to -- Special Master, with regard to the motion to disqualify, this one relates to AstraZeneca, and I'm not -- for some reason it is not wanting to -- let's see if I can get it to go down here. Well, it worked this morning. There we go. All right.

And specifically here with regard to the

motion to disqualify, Special Master, what I tried to do on this opening slide was really say for you really why this should be granted.

And here we have Dr. Moeckel's own statement, which is: "I am very interested in working with Ice Miller and Katherine," that Katherine is me, "on the interesting Astra[Z] legal cases."

And this, of course, statement was made by Dr. Moeckel a very long time ago at the very inception of this litigation when we were starting to look for general causation-type experts in this litigation, not knowing who our particular plaintiffs were, there was no bellwethers yet, we did not know about Mr. Rieder yet or Mr. Bales, but we were looking for general kidney pathologists and in particular human pathologists, and that's why I was reaching out to Dr. Moeckel.

So it's important here, I think --

THE SPECIAL MASTER: Okay. Can I --

MS. ALTHOFF: Yes, go ahead.

THE SPECIAL MASTER: You may have this already, but, I mean, we've looked at some of the case law, and, I mean, I guess one of the key issues is I saw in, I guess it was your papers, a consulting agreement

that he sent over to you.

MS. ALTHOFF: Yes.

THE SPECIAL MASTER: Was there ever a consulting agreement -- I mean, I assume in cases like these you have a standard consulting agreement that you sign with all of your experts.

Was such a consulting agreement ever signed by both parties or was -- did you ever sign the agreement that he sent over?

MS. ALTHOFF: So, that's a good question, and what happened here was Dr. Moeckel, and actually if we go to this next slide we should be able to get it here. So, in fact, that consulting agreement I think is up on the screen right now, and --

THE SPECIAL MASTER: Yeah.

MS. ALTHOFF: Yeah. And so Dr. Moeckel sent that to us and we responded with an e-mail that said, Yes, we absolutely would like to engage you as a consultant.

So did we sign the same document that he sent us, no. Instead we responded with an e-mail and it actually came from me. And then, thereafter, you know, in reliance on that we went forward and met with him.

THE SPECIAL MASTER: Do you have a copy of your e-mail in the PowerPoint here?

MS. ALTHOFF: Not in the PowerPoint, but it would be an exhibit to our motion, Special Master, because it would be attached to my declaration.

THE SPECIAL MASTER: Okay. And -- okay. Keep going.

MS. ALTHOFF: Yeah, sure.

So what happens next. Let's see here. I don't know why this is not advancing correctly. All right. There we go.

So I met with Dr. Moeckel. This was not simply a case as some of the ones that have been cited in some of the motion with regard to a single phone call or where you blast a bunch of experts with materials. This is not that case.

I actually flew to New Haven, Connecticut and met with Dr. Moeckel. I spent two hours in his office and I had a roadmap of things I wanted to talk to him about and met with him for two hours. We talked about everything from his background and expertise as a human kidney pathologist, not working for the plaintiffs in this case, but then also talked with him about who we had retained, who we were

thinking about retaining. These were not only experts that would ultimately be disclosed in this case but also consulting experts.

We talked to him about the plaintiffs, what we expected to be their mechanistic theories, we talked to him about our mechanistic theories, and at the end of that two-hour meeting, I asked him again if he continued to want to meet with us and he said he did.

And so I asked him what next steps would be, and he said, Please send me some materials, which I did. I sent him two binders of materials of literature, medical literature and scientific literature from this case, which ultimately I would say showed up on his materials considered list.

THE SPECIAL MASTER: Okay. Can I ask you a question?

MS. ALTHOFF: Absolutely.

THE SPECIAL MASTER: Was he paid? Have you ever -- has AstraZeneca ever paid him for any of the time he spent meeting or reviewing that literature?

MS. ALTHOFF: That's a good question. I mean, I will tell you no, we did not send him payment. He told us he would expect payment. He sent us his fee

schedule, which is in our papers, told us how much he would charge us.

As is the case often with these experts, until they get closer to writing their report they don't send a bill and he didn't. He didn't send a bill, he didn't tell me he didn't want to, he didn't tell me that he didn't expect to be paid. He told me he expected to be paid. He just never sent a bill.

THE SPECIAL MASTER: Did you ever ask him for a bill?

MS. ALTHOFF: Not that I recall. No, not that I recall.

THE SPECIAL MASTER: Okay. Okay. I mean, I'm just trying to go through the criteria that I think a lot of the case law has looked at.

Let me ask you, there is a long period, and I can see it on your -- on your timeline from '17 to '20. That's a long time not to be in touch.

Was there any contact between anyone on your side of the table with him in that roughly three-year period checking in with him, that kind of thing, any of that?

MS. ALTHOFF: No, and here is why. Dr. Moeckel was not going to be someone who looked at particular

bellwether cases and looked at medical records or even biopsies. We only have one case in the initial bellwethers that has a biopsy. And so really we wanted him to look at medical literature and give general testimony, if called, from a pathologist's perspective.

And so there really was no reason during that period of time to check back in with him. We had talked with him, we knew what his preliminary opinions were, and the parties were busy in the bellwethers taking depositions, looking at particular plaintiffs and that really wasn't going to be his role.

And I think the questions that your Honor -- that, Special Master, you are asking, really, go to the Syngenta factors or, you know, whichever type of case you want to look at, and whether we had an objectively reasonable belief that we had retained him.

And what I would say to that is, I think the best piece of evidence there is not only the consulting agreement that he signed, but also the fact that I reached back out to him in November of 2020. If I didn't think I had retained him, why would I reach out to him again and ask him to, you know, start

meeting with me to put together an expert report.

THE SPECIAL MASTER: Um-hum, okay. I think we found Exhibit D. And is this the e-mail that says:

"We thank you for your e-mail and fee schedule. Please do not hesitate to contact me or Katherine for any questions. We look forward to working with you and will be in touch."

Is that what you're -- I just want to make sure that's the document?

MS. ALTHOFF: I think so. There were several e-mails around that time, but that was -- yeah, that works.

THE SPECIAL MASTER: And when did you first -- maybe you have this in your timeline. When did you first find out that he was working with plaintiffs' counsel? I guess the expert report was submitted in 2021, right?

MS. ALTHOFF: Correct. Yeah, in April of 2021 we got his expert reports and I was as shocked as anyone to see his report in their stack.

We had reached out to him, you know, in November of 2020 and received back, I guess you would say a cryptic e-mail, which is only really cryptic in hindsight where he said he is not available for legal

consultation in the foreseeable future. But if we take ourselves back to November of 2020, I will tell you we were hearing that kind of thing from lots of healthcare providers who were busy with COVID or their organizations were limiting, you know, their contact outside of the hospital because of COVID. And so when I got it, I was disappointed because we were interested in working with him as a human renal pathologist, but I was -- it didn't tell me, Boy, I think he has switched sides. It never, never crossed my mind until I got the expert report.

THE SPECIAL MASTER: Okay. And then at that point what did you do?

MS. ALTHOFF: Well, we noticed his deposition along with, you know, all of the other experts, and I took his deposition.

THE SPECIAL MASTER: Okay.

MS. ALTHOFF: And asked him about it.

THE SPECIAL MASTER: And did you reach out to plaintiffs' counsel at that time to say, What's going on here or anything like that?

MS. ALTHOFF: No. We took the deposition and, frankly, I wanted to hear what the expert had to say with regard to, you know, was he going to say I told

them all along or any such thing. It was a bit of an awkward situation.

THE SPECIAL MASTER: Okay. I think we are down to about 15 seconds according to my timekeeper here.

Is there anything else that you wanted to add, take another minute or two?

MS. ALTHOFF: No. I think, you know, if you look at the situation, I do think we have an objectively reasonable belief that we had a confidential consulting relationship based on the facts here, and this is just not the type of behavior that this -- that the court should countenance. We think he should be excluded on this basis because this is -- you know, it's not going to look good to the jury when you see this and it looks poorly on the judicial process.

THE SPECIAL MASTER: Okay. Thank you.

Who is going to respond for plaintiff side?

MR. PENNOCK: Good morning, Special Master. Paul Pennock for the plaintiff.

THE SPECIAL MASTER: Hi Paul, how are you doing.

Katherine, we still have your screen up, I think.

Still up. There we go. Okay.

All right. Go ahead, Paul.

MR. PENNOCK: Thank you.

First, I probably -- I probably should say and remind the Special Master, at least, as you saw in the papers that we -- I did not know that this contact had taken place, so -- in terms of her -- in terms of her going to meet in Connecticut or anything of that type. I never had, therefore, any conversations with them about those discussions, neither did Bess DeVaughn or Tracy Finken who had been working with him. We knew that a reach out had occurred years earlier and that's it and we didn't question him about it.

THE SPECIAL MASTER: When did you start meeting with him, Paul? When did your team start meeting with him and did you ask him about, you know, whether he had been contacted by any other party?

MR. PENNOCK: So it was in November of 2018 that we first started having contact with him. I was not a part of that at that time. And there was -- as I understand it, he did say the other side reached out to him a couple of years earlier and that's the extent of it from what we knew.

You know, the further exposition of the contact all happened at the deposition. You know, I was surprised by it, on the one hand, but on the other hand I'm glad I hadn't had any discussions with him about it.

So he had really no recollection of it. He didn't even recognize counsel that had been at this meeting. I mean, counsel has testified that it was a two-hour meeting. You know, I don't know that that's borne out. But in any event, he had really no recollection of it, any materials that were sent he did not have, and as far as he was concerned it all ended almost as fast as it began.

And to -- so that's sort of just the context that we were not understanding what had occurred with respect to that until the deposition took place.

I -- you know, we were not told when the report came out what had happened. I can't really lay too much fault at that. You know, I'm just, like, look, she wanted to come him and question him cold on it, take me by surprise, well, that worked, she did.

And I don't lay a lot of blame there, but I think the fundamental issue, at least the first

fundamental issue is whether or not there was this contract. I suppose someone, particularly lawyers, somehow could read into that responsive e-mail that there was a meeting of the minds to form a consulting relationship. I mean, I would suggest it's ambiguous at best, sending that to a doctor saying, he says I'm very interested in going forward and then -- and working with Ms. Althoff and then they respond, We look forward to working with you.

You know, I can tell you that certainly from Dr. Moeckel's point of view, he did not have a consulting relationship with them. They had left it there. They never went forward and they did not sign the document that he sent to them asking them to sign, which to him, you know, you can see why to him that would indicate they don't want me. I've sent them my deal. They've not signed it. They just sent me an e-mail and that was the end of it. So --

THE SPECIAL MASTER: Was that a stated -- his stated position, that he did not think that he had a -- he had been retained by him?

MR. PENNOCK: He absolutely did not think he had in any way been retained by them. He didn't even review the literature that was provided to him. And

the reason is because there was no follow-up on what he asked them to do. I mean, he took the initiative to say, Here is my deal, this is my consulting deal with a signature line and it never came back.

So then in the intervening time period, of course, we are doing the same kind of reach out and we get in touch with him.

And I just want to note a couple of other things, Ellen. Again, I'm sorry. I'm regurging (sic) -- regurging the papers a little bit, regurgitating it. They didn't have him sign a protective order, they didn't have him sign any confidentiality agreement, they didn't make any payments, those things that you were asking about.

And so this, to me, is sort of the same type of instance that I've had myself, where I've reached out to somebody and had a conversation with them and they said, Oh, thank you, and then they never responded to my further inquiries and then they show up on the defense side. That's happened more than once, several times. And I don't think that it in any way compromises or reflects badly on the integrity of the trial process because these conversations took place. And, you know, whether --

THE SPECIAL MASTER: I thought I read in someone's papers that there was a notebook of studies that was given to him with, I don't know what the number is, like 30 studies, and that in his -- his report that he did for plaintiffs he utilized, I don't know, 28 of them. I might not have the exact numbers right, but I thought I read that.

And doesn't that indicate that at least -- at the very least he looked at the materials that the other side had culled for him?

MR. PENNOCK: No, and the reason is because these are materials in common. These are publicly available published literature which are -- you know, there is a certain volume, as you know, of literature that's always, you know, revolving around the core issues in a case and these were some of those articles, particularly as they concerned the issues on both animal and human pathology. And so we had the same selection that they had or some portion of the same selection.

So that was overlap due to the fact that these are, indeed, the articles that you would provide to somebody to take an initial look, but I don't know, other than what they've told me, what they sent to

him, because he did not have it.

And after the deposition, that was one of my first questions: Do you have anything still? And he did not.

So -- so that is -- you know, if we looked at really any of the experts, I think Special Master, you know, whether -- if you look at a nephrologist, a general causation nephrologist, if they had one, you would look and you would see they have all of the same epidemiological articles. It is in that vein and I would suggest that it's -- to say it's common would be an understatement. So he did not utilize what they sent him in any way.

So I don't think that the integrity of the trial process is in any way reflected upon -- or badly reflected upon because of this. It was really, I think, innocent on both our part for sure and -- and I would suggest equally for sure on Dr. Moeckel's part. He is a doctor. He didn't think he had any agreement, we hadn't heard from them in two years and we reached out to them and he said, Okay, I'll take a look at what you want me to look at, and it proceeded from there.

You know, if -- I think that the court has

seen -- you've seen, Special Master, there needs to be specific and unambiguous confidential disclosures, I don't think there is any record that that took place.

And so if you take this record on its whole, I would suggest, I really don't think they even get close to being able to disqualify him for these communications that happened. He didn't think he had an agreement, he didn't look at anything they had, he doesn't even remember the meeting, he didn't even remember Ms. Althoff who was sitting there across the table from him, and furthermore, we had a span of two years until he consulted with us and another two years before they reached out to him again.

You know, to suggest that, Well, we just really didn't need to talk to a pathologist until four years later, okay, I would say that if you have a real relationship with an expert of any caliber, let alone a world class expert like this and you really wanted to work with him and you thought you had a relationship with him, you would have had some contact in between and had provided some payment to him for whatever work you thought he had done, although they never checked to see if he did the work that they thought he was doing, which was reviewing these

literature articles and, in fact, he had not been.

So I think that if you look at all of the case law, it just really doesn't cross the bar in terms of disqualifying this expert that has done a massive amount of work on behalf of plaintiffs in this case. Thank you.

THE SPECIAL MASTER: Thanks, Paul.

Katherine, do you want to respond?

You are muted, Katherine.

Can you unmute her?

Can you unmute yourself, Katherine?

MS. ALTHOFF: Yep, there we go.

THE SPECIAL MASTER: Yep, there we go.

MS. ALTHOFF: Yeah, I don't want to regurgitate what we've already talked about. Judge, just a couple quick points.

I mean, Paul's big point was really the doctor sent her a consulting agreement and she didn't sign it and so he didn't believe that there was any relationship. Unfortunately that sort of belies the timeline.

The doctor sent the consulting agreement in 2016 and then I met with him for two hours after that, two months after that. So, you know, I think

that the fact, you know, whether we signed the agreement or whether we sent him an e-mail saying, Yes, we want to work with you and then I met with him for two hours, I think, is -- it certainly does not make -- does not break the case for sure.

Paul also raises the issue that there was no protective order sent to Dr. Moeckel. Well, of course there was no protective order yet in the case at that point in time. And we didn't send Dr. Moeckel any confidential records designated in the case, in other words, we didn't send him any of the plaintiffs' medical records, so there was no reason for him to sign a protective order. And once again, that is not dispositive of the issue.

And, you know, finally, there were a number of assertions made about whether, you know, what Dr. Moeckel told them and what Dr. Moeckel's impression was during the deposition. None of this is evidence and it is not in the record. There is nothing in the record with regard to whether Dr. Moeckel told the plaintiffs that he had been previously retained or didn't or what his contacts were. In fact, I heard for the first time today that he told Paul that he had -- had a reach out but didn't

disclose the two-hour meeting. That's all news to me and it's certainly not in the record. And this, you know, he didn't know who I was. I think he did know who I was at the deposition, but regardless, that's not in the record that he didn't.

So, again, I think these --

THE SPECIAL MASTER: Can I ask one more question of you?

MS. ALTHOFF: Sure.

THE SPECIAL MASTER: Do you -- I mean, do you have a standard consulting agreement that you normally give to your experts, I mean, because the one that he has that's there doesn't look -- I've done a lot of consulting agreements over the years -- doesn't look like any that I would normally have done. I mean, do you -- is that something you normally would do if you were going to use the expert?

MS. ALTHOFF: Not necessarily. At the beginning stages of an expert consultation, I typically meet with them, I often retain them via e-mail and then at some point in time sometimes I will provide a more complex one, but not necessarily. And certainly with regard to the experts in this case, in this MDL, not all of them have, you know, big, long complex

consulting agreement. It's -- I just -- I don't necessarily do it. I don't think it's necessary. And so, no, I wouldn't typically sign his agreement, which is why, you know, we retained him via e-mail.

THE SPECIAL MASTER: Okay. Thanks very much to both sides.

And I guess now do we want to move on to a discussion of your motion to exclude testimony?

MS. ALTHOFF: Sure.

THE SPECIAL MASTER: Okay. Are you going to do that too, you and James?

MS. ALTHOFF: Yes. Let me just advance through here.

THE SPECIAL MASTER: By the way, while you are doing that, I just wanted to ask that to the extent that anybody is using slides, using PowerPoint slides in -- in connection with their arguments, can you, when the arguments are done, send those to me, please, by e-mail, I'd appreciate it.

MS. ALTHOFF: Sure.

MR. PENNOCK: If we could get a copy as well.

THE SPECIAL MASTER: And send that to opposing counsel as well.

Yeah, I was just going to say that, and to

opposing counsel as well.

MR. PENNOCK: And the court reporter.

THE SPECIAL MASTER: And the court reporter, obviously, as well.

Okay. Go ahead, Katherine.

MS. ALTHOFF: Great.

Special Master, again, Katherine Althoff on behalf of AstraZeneca, and again, I believe James Mizgala is going to be maybe adding some comment on behalf of Takeda.

So pivoting from the motion to disqualify to the motion to exclude, and, again, on this first slide what I tried to do was sort of sum up in a sentence why our motion should be granted and why Dr. Moeckel should be excluded.

And here, specifically, Dr. Moeckel testified that his job in this case for the PSC was to review pathological findings, if any, in the kidneys of test animals. So, in other words, he was retained to be an animal pathologist. And when asked at his deposition about that, he told us: "I am not an animal pathologist."

It's really pretty simple. Is this a qualifications case? Sort of. But what you really

find out is that because he is not an animal pathologist and because this isn't what he does, he has done some testing, but this isn't what he does in his ordinary life, he did not have a reliable methodology that he used, and ultimately his qualifications don't fit. And then, lastly, of course, we can get to the fact that if, in fact, he can render testimony about what he saw in the slides of animal kidneys, he has testified he can't link that up to humans. And it's just simply his observations of what he saw in the animals.

And, unfortunately, plaintiffs have nobody else. This is a little bit like Wells, but here --

THE SPECIAL MASTER: Can I ask a question?

MS. ALTHOFF: Uh-huh.

THE SPECIAL MASTER: Can I ask a question. I mean, you are saying he is a human pathologist, not an animal pathologist, but we -- and God knows I'm a long way from being a pathologist, but don't we often in these kinds of situations regarding drugs, we look at animal pathology data because it provides some information that might or might not be relevant to -- to humans.

So, I mean, I just -- I wonder, you know,

and maybe I'm wrong about this, but that a pathologist who can look at human path slides probably could look at animal path slides as well, especially in this context where we do use animal data all of the time in evaluating drugs?

MS. ALTHOFF: Yeah, that's -- that's a very good question, Special Master, and here is why that's not the case here: Because the key issue here is a condition called "chronic progressive nephropathy." Chronic progressive nephropathy, if you look in the textbooks, is a rat-specific or for sure a rodent-specific disease.

So if you only look at humans and if you only look at human pathology, you've never seen chronic progressive nephropathy. And, in fact, Dr. Moeckel has never seen chronic progressive nephropathy. And as a human pathologist that is not surprising.

However, here the key testimony and the critical issue is AstraZeneca and Takeda, in their animal studies, reported to the FDA that what was seen in terms of findings on the kidney pathology was chronic progressive nephropathy.

Now, Dr. Moeckel, who has never seen it

and who is not an animal pathologist, wants to come in and testify, Oh, I looked at those slides and I did not see chronic progressive nephropathy, the rat-specific condition. That requires an animal pathologist.

THE SPECIAL MASTER: Let me ask you another question. I mean, you were -- you either retained him or were considering retaining him, as we've discussed previously.

What -- why if he is -- why if he is someone who is not qualified to give an opinion in this case?

MS. ALTHOFF: Oh, I'm not saying he is not qualified to give an opinion in this case. We wanted to retain him and did retain him as a human pathologist. So to testify as to what, for instance, acute interstitial nephritis looks like in a human on biopsy. And as a human animal -- or excuse me -- as a human kidney pathologist, you know, what drug-induced interstitial nephritis looks like and what causes it.

That's not what he is doing here. Here he is looking at rats and dogs and he says he has never looked at a dog before, and telling you what he sees on the slides and whether it is consistent with a

rat-specific condition or not. And his testimony is it's something else.

THE SPECIAL MASTER: Okay. Thank you.

Anybody -- is James going to address this or...?

MS. ALTHOFF: Yeah, I'm happy to have James comment as well.

THE SPECIAL MASTER: I didn't know. I didn't know. I'm just asking. If not, we can go to the plaintiff side.

MR. MIZGALA: Just quickly, Special Master, this is really very similar to the Wells situation. I mean, again, you have -- you have this expert who says I've done -- I've looked at all of these slides and made mental notes about them and -- and then -- I can't -- but I can't tell you what that means with respect to humans.

I mean, if you look back, yes, there are cases where, you know, animal testimony -- or testimony regarding animal studies has been allowed in cases, but that's where somebody says, Oh, and what that means with respect to the humans having a condition is it's more likely than not or something. There is some sort of expert opinion tethered to that

analysis. We don't have that here.

The plaintiffs have conceded that he is not opining that the use of PPIs causes CKD in humans. He is not opining that the animal findings prove that PPIs cause kidney injury, and he is not opining on mechanisms of PPI toxicity.

Again, so what's a jury to do? They want -- they want -- and none of their expert -- other experts say, Oh, I looked at what Dr. Moeckel did and that's -- and that -- and what it means is this in my analysis of causation. We don't have that anywhere.

So, again, we are left with the jury speculating as to what these animal findings mean.

Thank you.

THE SPECIAL MASTER: Thanks.

Okay. Who is talking for plaintiff side? Paul, is that you again?

Okay. It's Paul.

MR. PENNOCK: Thank you.

THE SPECIAL MASTER: Can you unmute, Paul. You are muted.

MR. PENNOCK: Oh, I'm sorry.

THE SPECIAL MASTER: There you go.

MR. PENNOCK: Oh, okay.

THE SPECIAL MASTER: No problem.

MR. PENNOCK: I guess I'll just first quickly address what I -- the qualifications assertions that defendants are making.

It is in the record, Special Master, and it is certainly in our brief, Dr. Moeckel is extensively experienced in animal pathology and conducting research regarding animal pathology and including rats. There has made -- much has been made, as it often is, sound bites here or there, he had not seen CPN in rats, and that's a very relevant lack of finding by him because he has always been -- or almost always been dealing with younger rats. And the position and one of the bases of his opinions, that these lesions he is seeing in the Takeda and AstraZeneca younger rats are not CPN is because you don't see it in younger rats. And so if you are looking at these lesions, and he had other pathological features, histopathological features that he didn't see in these lesions, then that's -- that's the point. You see these lesions in older rats.

And so the fact that he hasn't seen older rats very often and, therefore, he hasn't seen a lot of CPN. But that's a little bit of a side note.

The qualifications, I think, you know, best might be summed up at Page 18 of the brief. I know you probably don't want me to regurgitate this, but I think it bears pointing out. You've had -- I don't know how anyone could have possibly read all of this briefing.

THE SPECIAL MASTER: It is a lot of paper, for sure.

MR. PENNOCK: It is the most paper I've ever seen, I think.

You know, the Yale University has named a research laboratory after Dr. Moeckel, the Moeckel Lab, where: Students doing post docs are exposed to a wide variety of physiologic, biochemicals, cell biological, molecular and cell biology experimental protocols, as well as different transgenic and knockout technologies to generate animal models for tubular injury regeneration, end quote. And this is the mission statement of the lab created at Yale and named after Dr. Moeckel.

Moreover, this is also a quote: "The student will be exposed to human kidney biopsy material in an attempt to correlate findings in the animal and cell culture models with actual

pathology" -- "or pathological mechanisms in patient kidney biopsy tissue."

So, you know, the rest of the record is replete with his qualifications that I think are really about as strong as you can get, which is borne out by his CV and all of the work that he has done which has included a great deal of animal work.

In terms of the next issue that has been raised, which is -- I think by James -- kind of hit the point most pointedly, Dr. Moeckel is coming in to testify, as histopathologists do, that -- let me withdraw that, Special Master. Let me approach it from the other direction.

What if the only evidence in this case were all of the animal studies from two different defendants were looked at by pathologists and there were no findings of any lesions that might be correlated with a human lesion, that the only findings in all of the pathology were chronic progressive nephropathy in the rats and that only has to do with rats, what if that were the only testimony in the case? That would be a big issue for any case where you are claiming that a compound has caused a toxic effect in a human in the kidneys.

So what do we have? We have an expert who is coming in to say, No, hold the phone. That's not correct. When I look at all of this pathology, I do, in fact, see lesions that -- in these rats that are not chronic progressive nephropathy that appear to be a tubular interstitial nature -- type of histopathology, lesion, and in addition I've seen evidence in these slides that that injury has, in fact, caused chronic kidney disease in the rats that's unrelated to chronic progressive nephropathy.

I mean, to say that that has no --

THE SPECIAL MASTER: How do you -- how do you link it, though? I mean, I think the question that Takeda's counsel, James, was raising is who is going to link that testimony on the part of, you know, Dr. Moeckel to an effect in humans? I think that's the point -- at least a point that James was making that, you know, it is all well and good to talk about what happened to the rats, but how do you link that to impact on humans?

MR. PENNOCK: Very good. So to answer that specific relevance question, but I think there is another relevance point, both of our experts, both Dr. Charytan and Dr. Fine, have, of course, applied a

Bradford Hill analysis to causation, general causation of these -- of this disease entity with these compounds. And both of them in walking through the well accepted Bradford Hill approach and criteria have identified that in addition to all of the clinical evidence that we see, in addition to the evidence that we see in clinical trials, in addition to the evidence that we see in the many case reports, in the case series and, of course, all of the epidemiological studies that have come out, in addition to all of that, there is evidence of -- of an effect in animals and they will say and have said and it is something that is routinely testified to that when you are assessing human causation, you do look to the animal to see what, if anything, was occurring in the animal regarding the organ of interest and the disease of interest in the animal.

And it's -- and in some ways it's -- it is a matter of looking at it to see if there is nothing, because if there is nothing, as I started out, if there is nothing in the animal evidence at all and it's a competent body of animal evidence, that certainly raises a question in a Bradford Hill analysis of, if we are having this effect in humans,

why is there no biologically plausible preclinical evidence that we are seeing in the animals or in vitro, why does that not exist.

And it confounds, without the animal evidence or the -- and/or the in vitro evidence, it somewhat confound the Bradford Hill method or, I'm sorry, analysis of all of the evidence that exists. It certainly raises a question if there is no animal evidence that needs to be explained by the doc -- the medical doctors who are giving -- who are giving causation opinions.

So -- so the importance of the animal evidence and the fact that there are some indicia of renal toxicity in the animal reports that these other experts read does -- does play a role in the evaluation of causation. And I say these other experts, I -- it was either Fine or Charytan that went through this -- went through this evidence or both, and probably Stephanie can answer that, but it's part of the Bradford Hill. So that's how it is connected up as to the relevance for human causation. It is in the general causation piece.

In addition -- and I hope that's answered, that question or at least --

THE SPECIAL MASTER: It answers it, yes.

MR. PENNOCK: -- or at least appears to, okay.

So the second, I think, relevance consideration for this evidence is, of course, in the conduct of the company, not just in what should have occurred when you have -- if you have properly evaluated your animal evidence, what should have been occurred -- what should have flowed from your identification of possible renal toxicity of a chronic nature in your animal models, other than something specific to the animal model.

Well, if that comes out, if you find that, if you identify it, if you properly evaluate it and assess it, then you should, and I think we see this throughout Dr. Ross's description of what happened here, that should give you some kind of signpost on the road, not that you don't put the drug on the market, not -- not that you're -- you're going to put in a warning of renal toxicity when you launch of the drug, but it is a signpost that, you know, there might be a bridge out ahead and -- and so now you are alert, which is why we do animal studies, first we do them to see if something ridiculous happens, like they all get cancer and die, but really, we are looking to create

signposts of what might happen in the clinical setting, what might happen postmarketing. And so if we had properly done our work, we say, Oh, there might be some renal toxicity in there. Oh, that might be relevant to humans.

Well, guess what, you launch the drug and suddenly you are getting case report after case report published in reputable journals saying, Hey, I just had a -- I had a patient, two patients, three patients, seven patients, which is what happened, as I think the Special Master knows, throughout the '90s, of renal effects and ultimately chronic toxicity. Well, that's why those signposts exist in the animal studies and that is the other relevant aspect of Dr. Moeckel's testimony in this case and in any case.

THE SPECIAL MASTER: Okay. Thank you, Paul. I think our time is up.

MR. PENNOCK: Thank you.

THE SPECIAL MASTER: I think you might have a few minutes for rebuttal if Katherine or James want to say something.

Katherine does, okay.

MS. ALTHOFF: Yeah, just a couple of quick points.

Paul identifies on Page 18 the extensive animal qualifications of Dr. Moeckel. What's very important here is Dr. Moeckel, to the extent he works with animals, he works with models of injury of animals. So where they try to take an animal and simulate what they see in humans. So they'll clamp off a kidney and simulate acute kidney injury. That's what he does. That's why he is not seeing chronic progressive nephropathy.

What he has a very, very little experience at all in is toxicity studies where you take an animal, you give them a drug and you see what happens. He does models of kidney injury. It is a totally different deal than -- than he does within toxicity studies.

Next, with regard to the link up, if there is a link up, it's not in the record. I saw nothing in the plaintiffs' briefs that say Charytan relies on Moeckel, there is nothing that says that Dr. Fine relies on Moeckel. I'm not aware of that.

So, you know, do they talk about animal evidence? I'm sure they do, as does their other expert Dr. Smith who reviewed AstraZeneca's own preclinical filings with the FDA and reached certain

opinions about that. And there is no Daubert motion pending on Dr. Smith.

But what we are talking about here is Dr. Moeckel reviewing slides that he is not qualified to do and didn't use the correct methodology to do and then nobody relying on him to connect that up to what does that mean for humans.

THE SPECIAL MASTER: Thank you.

James, did you want to add anything?

MR. MIZGALA: No. Well, just, you know, Ms. O'Connor earlier pointed out when talking about Wells, you have to have somebody connecting the dots and that is just not happening here. No one is saying I -- I took Dr. Moeckel's analysis and that means that I can use that in my Bradford Hill analysis. It is just not happening.

THE SPECIAL MASTER: Okay. Thank you. All right.

I guess where we are now is Ross, is that right? And who is going to speak to that one?

Okay. Mr. Horowitz.

MR. HOROWITZ: Yes.

MR. RUTTINGER: Also Mike Ruttinger for Takeda.

THE SPECIAL MASTER: How are you?

MR. HOROWITZ: Good. How are you?

THE SPECIAL MASTER: Good.

MR. HOROWITZ: So, Special Master, again, Jeff Horowitz, Jeffrey Horowitz on behalf of AstraZeneca and I'm going to argue the motion to exclude plaintiffs' regulatory expert Dr. Ross, along with Mike Ruttinger, who is going to speak on behalf of Takeda, as he said.

I know that you are more than well versed in the world of Daubert and FDA expert or purported FDA expert testimony, so I think -- you know, I think we can --

THE SPECIAL MASTER: I have done a little of that work over the years, yes.

MR. HOROWITZ: Yes, I am well aware.

THE SPECIAL MASTER: And, I mean, I want to start out by saying, you know, you really -- you aren't really disagreeing that Ross is qualified as an FDA expert, are you?

MR. HOROWITZ: Not as an FDA expert, of course not, no.

THE SPECIAL MASTER: All right.

MR. HOROWITZ: This is a unique -- you know, it seems that in today's day and age, you know, everybody

wants to talk about Parisian and the Trayslol opinion and courts tend to try to find ways not to go full, you know, full Parisian Trayslol.

I think this is a unique situation, a unique case, and that may just be merited here for two reasons. No. 1, you have a stunningly fulsome regulatory record on the very issues that are at the core of these cases. It's -- it's going to be laid out, I think, in some detail more for you tomorrow when William and Mike argue preemption, but you can't get away from it.

And then the second piece is the absence of fit, I think, is really stunning here as well, which is the real opinions that Ross purports to offer don't really fit the facts of these cases where the claim is really for CKD and yet he really doesn't opine, certainly not clearly, that that's what was missing from the label. He talks about ATIN and CTIN in this mythical reference to sequela that really has no support in what he cites.

THE SPECIAL MASTER: Yeah, I think -- can I just say I think there is something, and maybe when it is his turn to speak we can address it, of a disconnect here about exactly what they are claiming should have

been disclosed, warned of, et cetera.

I mean, it seems to me that ATIN and CTIN are distinct from CKD. But you don't dispute, do you, that they can lead to -- to CKD and that's why they are relevant?

MR. HOROWITZ: I don't know that -- I don't think it's as clean as you are suggesting, which is what plaintiffs and Ross would like that to be the case. And the best, I think, answer to that is in the FDA's review analysis, particularly in 2019 and 2020, or really even post 2016, once you get the -- the Lazarus literature report, because the CKD is unique and it is a defined renal injury that is separate and apart from CTIN and ATIN.

And I think this really underscores the problem with Ross's report, which is he is not the person to make that connection and it is certainly the methodology that he applies to try and make that connection through this prism of, Well, I'm the regulatory guy, so I can -- I can -- I can make that connection. It doesn't work. You can't do it.

Let me -- let me -- if it's okay, Special Master, I want to start with some context on Ross, which is --

THE SPECIAL MASTER: Okay.

MR. HOROWITZ: -- you may recall he came in to replace, you know, Dr. Kessler when Dr. Kessler went back to the company, we can talk about that separately, and he comes in on March 15th. Two months later he serves a report that is 274 pages long. And that is sort of one of the mantras, if you look at the plaintiffs' opposition brief, Well, you know, I wrote this 274-page report in two months. And when I asked him, this is Page 117, Line 24 of his deposition to Page 118, Line 5:

"Before you were retained by the lawyers in March of this year to provide a report on May 15th of this year, I think I told -- I think you told me you didn't know anything about PPIs and CKD, right, that's what you said?

"Answer: I think that's a fair statement."

So he comes in, and in two months purports to do a comprehensive fulsome regulatory review of this record that has been subject to scrutiny by FDA for the number of years it has been, it's -- the contrast between reality and the role that Dr. Ross is purporting to play is stunning.

And then the second piece is, you know, it has become popular for the FDA experts to sprinkle this sort of like, I call it the ipse dixit fairy dust of, Well, I was an officer at FDA and so I just applied the same methodology, you know, that I would have had I been at FDA.

Well, of course they are going to say that, but the real question is: Did they do it, did they really dig in and review the materials and actually apply the regulations and explain how they are applying the regulations.

And it is eminently clear from Dr. Ross's report, and then, you know, his deposition, frankly, he almost makes Parisian look responsive. You know, you've got to alligator wrestle him on every single question. The reality is he cites the kinds of materials, I'm not going to dispute that, that you would expect an FDA officer, you know, medical officer or medical reviewer to look at. Of course he does. But there is no explanation as to how he truly applies the standards. It is really just a recitation of studies, adverse event reports, case reports and then there is an immediate leaping to these conclusions, you know, arguing the plaintiffs' case, the oath

swearer testimony, if you will, that doctor -- and that the Judge Kapel (phonetic) pointed out way back when. I mean, that's really what this report is.

And then, if you actually contrast what he says and in, you know, the opinions that he offers with the actual record, the documents themselves that the jury can look at, the jury can review, you know, he offers this idea about severe sequela that should have been in the label even pre 1996 even in the context of acute IN.

Well, the 2014 label change, the FDA specifically, in response to the citizen petition specifically chooses not to include that language. He may disagree with it, but he doesn't even address it.

THE SPECIAL MASTER: I have a question on that.

Isn't the point, I think, that plaintiffs are making, and I think you -- again, I think you guys may be talking past each other to some extent, is the plaintiffs' point I think is that a warning about ATIN and CTIN would highlight that there is a risk to -- there is kidney toxicity, there is a risk to the kidneys and, I mean, he does, in quite some detail in his report, and, you know, I don't know how it was put together or whatever, but he goes through and refers

to all of these earlier reports, challenge, rechallenge stuff, and concludes from that that an earlier warning was required.

I mean, I do think, you know, whether you agree that he -- he dug into the data the way you would like him to or did the review you would like him to, I do think that's the point he is making, is it not?

MR. HOROWITZ: I agree that's the point he is trying to make, but the manner -- it is the methodology, the manner in which he gets there is deficient because he doesn't explain, he doesn't say how he leaps from, you know, a discussion of a single dechallenge -- rechallenge, dechallenge case to reasonable evidence of a causal association.

And in particular, again, he mixes -- I think one of the great examples I wanted to show you, and it is not really set forth directly in the papers, if you look at Paragraph 598 of his report, which is something that the plaintiffs cite in their opposition on Page 9 and emphasizing exactly what you just referred to, if you look at what he actually says, he says that:

"A warning of a risk of acute interstitial

nephritis with the potential to cause permanent renal impairment, including chronic kidney disease, should have been submitted before 1996."

Respectfully, that makes no sense. And, again, you know, CKD is separate and apart, it is distinct from ATIN and CTIN and it's just a perfect example of what's happening here. It is just leaping to these conclusions, mouthing the regulations. I mean, any -- any -- any regulatory expert, even Parisian now knows that you have to mouth the words "reasonable evidence of a causal association" and, you know, to cite to 201.57, but you've got to lay it out, you've got to explain how you get there.

And the problem here is he is doing it in the face of an FDA record like the 2014 label change where exactly what Ross is saying was not included, the sequela, and he doesn't even address it.

And then you have the 2017 TSI conclusion. I mean, it is publicly available. And I asked him about that also at his deposition. He didn't even know about it, and he doesn't address it in his report where the FDA's TSI review concludes specifically no action is necessary with respect to CKD.

And then you get to 2019 and '20, and

although he cites to some of the documents and purports to put forth a regulatory record, it is cherry-picking and he doesn't address head on the documents that say 180 degrees the opposite of what he says.

That's not a methodology. He just ignores the fact that there are statements by FDA, by the epidemiology group that's doing the review, by the TSI group that's doing the review, that specifically says, We have a reason and a rationale for not offering a CK -- or for not including a CKD warning. He just ignores it.

That is ipse dixit on steroids, that is Joiner, it's a gap, it is an analytical gap.

THE SPECIAL MASTER: Okay. I think -- I think we've got -- we called time.

Who from plaintiff side is going to address?

It looks like Paul again.

MR. PENNOCK: I will, yes.

MR. HOROWITZ: I'm sorry. Did I take Mike's time as well?

THE SPECIAL MASTER: Oh, I'm sorry. I apologize. I forgot. Sorry, Mike.

MR. RUTTINGER: The Takeda motion is a separate motion, Special Master, so we can do it in whatever order you want.

THE SPECIAL MASTER: No, no, no, go ahead. I think it's better -- Paul, unless you disagree, I think it is better to let defendants have their say and I think it will abbreviate things if you can respond to both together.

Is that okay?

MR. PENNOCK: Yes, I absolutely agree to that.

THE SPECIAL MASTER: Okay.

Go ahead, Mike. I'm sorry.

MR. RUTTINGER: Good morning, Special Master, Mike Ruttinger for Takeda. I'll try do keep it fairly brief because Takeda's motion is confined to the Bales case, but there are a couple of unique issues relevant to the Bales case that are kind of implicated by some of your questions that I think we can had address.

So I want to begin with Takeda's fit argument as to Dr. Ross's testimony in the Bales case.

Special Master, you raised this question that a lot of the issues implicated by plaintiffs' opposition to the Daubert question is, you know, this kind of blurring of lines between acute TIN, chronic

TIN and chronic kidney disease. And I'm going to share a slide here that reflects Dr. Ross's testimony on this point that I think helps to address this.

So chronic kidney disease is a distinct kidney injury characterized by an irreversible loss of kidney function over 90 days. In this it is distinct from the other kidney injuries discussed by the plaintiffs in Dr. Ross such as acute kidney injury, TIN, acute TIN, chronic TIN, and this is a fact that Dr. Ross himself acknowledged during his deposition testimony.

Now, I want to emphasize this distinction because Dr. Ross also said the first published report in evidence associating a distinct condition of chronic kidney disease with PPIs did not come out until 2016.

Well, with respect to the Bales case, the last instance of Plaintiff Freddy Bales's use of Takeda's product was 2007. So to the extent that Dr. Ross's opinions about CKD are premised on evidence that doesn't come out until nine years after Plaintiff Bales used -- last used Takeda's Prevacid drug, it doesn't strike us that there is any actual fit between his CKD-specific opinions and the facts of

the Bales case.

Now, with respect to the evidence that has come out regarding Bales's own conditions, it is clear that --

THE SPECIAL MASTER: Can I interrupt you there for a minute, Mike?

MR. RUTTINGER: Of course.

THE SPECIAL MASTER: Can I interrupt you there for a minute?

I have seen that quote used many times in the papers, and, I mean, no doubt he says -- he says what he says. He says that the Lazarus, et al. studies were the first group of studies to report on the relationship between PPI and CKD, but if you look at his report, as the point I was making earlier, you go back to, I don't know, Paragraph 445, 443, somewhere around there, and he really does talk about earlier reports. And I think taking that one statement about 2016 is a little bit out of context.

Now, that may be the CKD versus ATIN and CTIN distinction that we've talked about, but I do think there is -- there -- and you can disagree with it, but I think there are statements in his report that suggest that risks were known earlier.

MR. RUTTINGER: So this gets to the second question I kind of wanted to address that you raised -- or Mr. Horowitz, I'm sorry, raised, which is the distinction between chronic kidney disease specifically and this notion that plaintiff advocates of a generalized notion of renal toxicity.

So if you look at the information predating 2016 and Lazarus that Dr. Ross looks at, he talks a lot about TIN and potential sequelae of TIN. But, again, those are actually clinically distinct conditions, whereas in most instances the evidence shows and the reports show that AIN, ATIN, CTIN, for example, are, you know, inflammation of the interstitia that actually is often reversible.

Chronic kidney disease as a distinct medical condition is actually considered to be irreversible. And so chronic kidney disease is also the only condition, not only alleged by Plaintiff Bales, it is the only one he has ever been diagnosed with, but I think most importantly to this point, no witness and no evidence in this case has ever attributed Plaintiff Bales's chronic kidney disease to any of those other conditions that Dr. Ross talks about, such as the TINs.

So the Daubert fit analysis, when you look at the case law, normally requires a nexus between the expert's testimony and the facts of the case, such that it is going to be helpful to the trier of fact in resolving that disputed issue. Dr. Ross's testimony, however, won't add anything to the discussion of CKD, at least in 2007, since he himself has admitted there is no reported association between PPIs and CKD before 2016.

Now, I do want to add a little bit to what Mr. Horowitz has already said about reliability, just kind of pointing this -- pointing you, Special Master, to a couple of the actual examples of this that I think are really quite fitting.

So, you know, plaintiff at length, as we discussed, in their brief details a lot of the materials that Dr. Ross looked at, case reports, challenge, dechallenge reports, but the Daubert reliability analysis requires more from a regulatory expert than just simply, you know, recite the standards.

So if you look at Dr. Ross's report, in Paragraphs 32 and 153, he acknowledges that both the newly acquired information standard and the causal

association standard. So 21 CFR 314.3 and 201.57. You are going to hear a lot more of those about that in the preemption arguments tomorrow. I'm not going to go into detail on that, but suffice it to say that both of those regulatory thresholds have to be met before a drug manufacturer can make a label change.

Now, Dr. Ross says, Well, the information I looked at is newly acquired information, but other than saying early on in Paragraph 153, newly acquired information as defined by the FDA is information showing a greater severity or frequency of risk, the rest of the report is silent as to whether any of those reports, studies or articles he cites actually show a greater severity or frequency of risk.

So if he is not doing a comparison of what he is alleging to a baseline of the knowledge that was already known, he can't support an opinion that that was newly acquired information meeting the regulatory threshold. So that, I think, is where in our view the reliability of his methodology breaks down is while he's cited the correct standards and he has looked at much of the information he might have looked at as a medical officer of the FDA, he has never -- you have heard several times today already -- connected the

dots. He never connects the dots between that regulatory standard and the data he is looking at and whether it actually meets the metric of a greater severity or frequency of risk. In short, he is skipping the most important step that as a regulatory expert you take, applying the regulatory standards that he learned and experienced in his time at the FDA to the data.

Now, I do want to mention just two more quick adjacent points on Dr. Ross specific to the Bales case. He does in his report express an opinion that in 1995 there was already existing information that would support a label change with respect to acute TIN. He says that information existed by the time that Takeda's Prevacid came on the market in 1995. So by definition, Dr. Ross's opinion as to acute TIN is related to a pre-approval claim, there is a lot of case law out there in the preemption context that more or less uniformly acknowledge that pre-approval claims are preempted.

So regardless of what else we said about Dr. Ross, we don't think that he should be allowed to offer that opinion as to ATIN with respect to the Bales case for Takeda.

And there are also a number of different areas within his report where he claims that Takeda was failing to carry out pharmacovigilance obligations under the regulations. It is very clear there is no private right of action to enforce those various regulatory obligations under the FDCA. So to the extent he is offering testimony that would suggest Takeda failed to carry out, say, pharmacovigilance obligations under the regulations, we think that's clearly preempted under a fraud on the FDA Buckman preemption theory.

So with that I'd like to reserve just a couple of remaining minutes for rebuttal. Thank you.

THE SPECIAL MASTER: Okay. Thank you. All right.

Paul, go ahead.

MR. PENNOCK: Thank you.

First, I think I have to note that I feel like I'm hearing a lot of new arguments and points in the two arguments by counsel. One I would just like to make mention of specifically, although there were quite a few, that is this seeming innuendo that somehow Dr. Kessler prepared all of -- you know, some substantial portions of this report because of when

Dr. Ross was engaged. It is simply not true, A, and, B, it is not part of the record, and, C, really should not have been in this record, this transcript shouldn't have been littered with that. I don't think it's something that should have been part of this discussion. I would move to strike it.

And Dr. Ross, hopefully he will testify at trial and when he does I think anyone attending will be struck by his brilliance. He is a -- he is a brilliant person.

In any event, so let's talk first about qualifications. You know, somebody mentioned he is a medical reviewer and so as a medical reviewer he, you know, claims he knows how to approach all of these pharmacovigilance issues.

Well, yes, he was a medical reviewer. He also rose to the level of Deputy Director within FDA in CDER. So, you know, his CV needs to be re-looked at, I think, and these statements as to snippets of his alleged lack of qualifications, although they -- I think they said at the beginning they are not really challenging his qualifications, so.

THE SPECIAL MASTER: I think my first question was: You are not really challenging that he is

qualified to be an FDA expert? And I think Mr. Horowitz said no to that, so, that they were not challenging that.

MR. PENNOCK: Okay. Thank you.

So I'd like to turn next to the methodology employed and described in the report regarding his evaluation of the evidence in this case.

He is initially looking at, in this entire body of evidence, as to whether or not there was a basis under the law, under the regs for a warning that had to be issued by these companies regarding anything about renal toxicity and, you know, well, these drugs and renal toxicity or chronic kidney.

THE SPECIAL MASTER: Well, that's something -- Paul, I don't mean to interrupt you.

MR. PENNOCK: That's all right.

THE SPECIAL MASTER: But that's something that, as I said earlier, I feel like there is a disconnect between the two sides on this, and if you can, I'd like you to state what exactly your failure to warn claim is. Is it just that the word, you know, "chronic kidney disease" had to appear? I mean, your expert seems -- Ross seems to say that ATIN and CTIN are things that should have been warned of earlier.

I mean, I do -- I think the papers talk -- I mean, at least having sat down and read them, they seem to talk past each other on that, and, you know, their points -- the points that Mr. Horowitz and Mr. Ruttinger were making were that -- that it is not the same thing, and I get that it is not the same thing, but I think it would be helpful if you could address sort of what exactly is your failure to warn claim here?

MR. PENNOCK: Absolutely, Special Master, and I was getting to that and I apologize I was unclear.

I was talking about we initially asked him, look at this evidence that exists and he applied his methodology to look at it and see if there were any evidence of renal toxicity and then I will talk about what he found. And I know exactly the question that you are asking, and I think I can adequately address it.

But as far as his methodology is concerned, I'll quickly say, it is laid out numerous times in the report at Paragraph -- he discusses it at Paragraph 69, 71, he discusses it at Paragraph 255, 120, 123, 270, 259, all of these places he discusses how, if you are trying to evaluate if there is

reasonable evidence of a causal association between a drug exposure and anything, these are the steps that you go through in looking at the evidence and the type of evidence that you looked at. And he did that.

I'm not entirely sure there is quarrel with whether or not he followed that particular method. It looks at temporality, biologic plausibility, mechanism of injury, similarity to other drugs, the, you know, nonclinical evidence, and then, of course, case reports and challenge, rechallenge and all of the things that we see in his description, but he laid out as a method that's what you do.

Now, I'll turn to the conclusions. So based upon his review of the evidence, Dr. Ross found that by 1995 there was reasonable evidence of a causal association that these drugs -- with these drugs and acute interstitial nephritis, also known as acute tubulointerstitial nephritis.

This is a disease entity or an injury entity that has been known for a very long time, it is associated with other drugs as well, prominently NSAIDs, and by 1995, and there is -- this is in the record throughout this case, by 1995 it was black letter medicine that if you suffer from a severe

enough case of acute interstitial nephritis, you can have damage to your kidney that will ultimately continue to compromise your kidney throughout your life and result downstream in chronic kidney disease. That cannot realistically be disputed by defense experts.

AIN, if it is severe enough, can cause downstream chronic kidney disease, that one event over a period of what, days or weeks, can happen. Okay. So he says, if you look at the evidence that existed to the companies, both internally and the published evidence, there is no question that there was a reasonable causal association between AIN and the use of these drugs and, therefore, that's why he mentioned, therefore, in his opinion the sequelae should have also been mentioned in a warning that should have gone into effect, that the warning should have said, reasonably -- these drugs potentially can cause AIN and AIN can potentially cause downstream chronic kidney disease, the sequelae.

Now, there is a final common pathway to chronic kidney disease that is itself a chronic kidney disease and that is chronic tubulointerstitial nephritis. The definition, as was mentioned earlier

by Stephanie, of chronic kidney disease when looked at by nephrologists, they look and they say, Okay, does my patient have an estimated glomerular filtration rate of less than 59 -- I'm sorry -- less than 60 and if he or she does I'll repeat it in three months and if it is still such I'm going to say she has chronic kidney disease. This is a clinical description of what's happening in a patient. But what the underlying process is for those instances, particularly in PPI, what underlying processes for certain drug-exposed cases and PPIs is chronic tubulointerstitial nephritis. It is a condition that is being created by the drug year after year after year after year and ultimately all of that reserve that you are born with in your kidneys has been destroyed and now you present to your doctor and you've got an eGFR of 58, 56. Now you are in that realm. It repeats and you've gone chronic kidney disease.

So the final -- but this -- so what -- what the process is from these drugs that results in that clinical diagnosis is chronic tubulointerstitial nephritis, and that is what Dr. Ross identified in the case reports that that had come out by the, you know,

approximately 14 or 15 of them, by early 2003. And in addition to the published reports, reports from a clinical trial, I believe it was from Takeda, in early '03. They found in the histopathology evidence of this chronic damage to the kidney that was occurring, it is called chronic inter -- tubulointerstitial nephritis. That's what it is. That's what was happening in a number of patients. That is what was identified histopathologically and that together with the other evidence that he describes in this section of his report is what led him to conclude that by early '03 a warning should have gone in place that said, these drugs, something along the lines, and I don't have the exact language here, but the -- these drugs have the potential -- these drugs potentially cause chronic interstitial tubulo nephritis.

Now, at that time, and this is important, and it was Riggs, and I think, Special Master, you pointed it out, I think, but in case we were missing each other, there had not yet been epidemiology that was extant that found an association between diagnosed chronic kidney disease in people at that time, that did not occur indeed until 2016. That's when the first published literature came out saying -- and by

the way, that published literature didn't happen by accident. It happened because of all of this other evidence that was building in the medical literature that the companies never warned about.

And so they go out and they look and they say, Hey, if these drugs really are causing an acute interstitial nephritis in a lot of people or if they are causing a chronic -- a chronic interstitial tubulo nephritis, then let's look at and see whether this is showing up in the diagnostic codes. You are not going to get diagnosed with chronic tubulointerstitial nephritis. You'd have to do a kidney biopsy and some pathologist will have to say that. You are going to get diagnosed with chronic kidney disease. So if you're going to say let's see if that's showing up in the epidemiology -- in the diagnoses of patients, then that's where the epidemiology came in. And they came in -- there is a plethora of it, as you know. Study after study.

THE SPECIAL MASTER: Can I ask a question, and we are almost out of time, but, you know, his experience is not as a nephrologist, right, Ross's experience, and, I mean, I think a lot of his argument and that you've described and that I've read is that,

you know, there -- these other conditions are -- result in chronic kidney disease or chronic kidney disease is a sequelae of these other conditions. And I think he is qualified as an FDA expert, but is he qualified to make that judgment and, if so, why?

MR. PENNOCK: Yes. And the -- well, the reason, it is multifactorial.

No. 1, if you look at his training and experience, I mean, this is an immensely qualified individual. We are talking about somebody that he -- you know, he got his bachelor at NYU in biochemistry, he then went on to -- I'm sorry -- bi -- he got his Bachelor of Science at Yale in molecular biophysics and biochemistry. Then he went on ultimately to get his MD at NYU, and went on from there to a fellowship at Yale in infectious disease. I mean, but the breadth and depth of his understanding of various aspects of science, medical science and -- and in particular internal medicine I think really can't be questioned.

Now, specifically, though, when you get to -- when you get to the FDA, you are working, they don't have -- they are not sitting around with nephrologists reviewing everything that happens or a

cardiologist reviewing everything that happens. When you are reviewing case reports that are coming out, adverse event reports and all of the other evidence that you mentioned that is relevant to a review as to whether there should be a warning, that is being done by various types of internal medicine doctors, typically, in FDA, which he did. You know, they are not specifically limited to the fields that they may have been trained and specialized in.

And one reason is, and this is the punch line, if you will, Special Master, they are not calling causation. I don't -- I would not argue that I could necessarily bring Dr. Ross in to say, These drugs indeed caused this problem. They are calling reasonable evidence of a causal association.

It is the very reason why Dr. Kessler has been approved and has testified so many times throughout the country in many different courts. He doesn't have -- he is not board certified nor does he even practice in many of the fields that he has testified in. He testified in our case in Actos that involved urology and bladder cancer. He has testified in cardiology cases, he has testified in -- probably I can't name them all, but I know you realize, Special

Master, that when you are a regulatory expert, are you trained to evaluate evidence, scientific and medical evidence to come to an opinion on reasonable evidence of a causal association, which is a step down from saying: In my opinion to a reasonable degree of medical certainty that drug caused that problem. And he will not be giving that ultimate opinion. He is giving the ultimate opinion on the regulatory issue of was your duty to warn triggered, was there enough to trigger that warning. And that's what he did, forgive the expression, all day long when he was at FDA. I hope that at least begins to answer your question.

So I don't know if I'm out of time, Special Master.

I think you are on -- let's not mute the Special Master.

MR. BROWN: Ellen, you are on mute.

MR. PENNOCK: You are on mute, Special Master.

THE SPECIAL MASTER: Okay. Sorry. Hi.

You are past time but that was because I was asking questions.

Mr. Horowitz or Mr. Ruttinger, do you want to give a short response.

MR. HOROWITZ: I would like to address very

briefly two points and then turn it over to Mike if that's okay.

THE SPECIAL MASTER: Sure.

MR. HOROWITZ: The first is I just want to briefly address the quote/unquote innuendo that Kessler wrote the report. I don't know how he got to that. That certainly was not what I was suggesting.

My only point was that he -- "he" being Dr. Ross slept at a Holiday Inn in the two-month period between when he was retained and generated his 274-page report and how that contrasts with the years and years of FDA attention to this issue.

Secondly, the other point I'd like to address is you asked very directly: What is your failure to warn claim and, honestly, Ellen, I'm still not clear, it was very -- it sounded very similar to what I heard from Dr. Ross during his deposition, but suffice it to say, and I think Mike laid this out clearly, our position, and it's the reality of the science and the medicine as reflected in the FDA reviews, that Dr. Ross does not address head on, CKD is a distinct condition and this idea that ATN with -- ATIN with sequela or CTIN is somehow the same thing is not true, that's not the science.

And, you know, that -- I guess I'll leave you with this, Ellen, it is very much like when I was fussing with Dr. Ross or he was fussing with me about the 2020 label change and where that landed. And, you know, he said, not basically, he clearly said, I asked him: Do you think FDA doesn't know the difference between CTIN and ATIN for purposes of labeling, and he said: Yes, they don't know what -- they don't know. And that's just ipse dixit. That's just a -- perfectly sums up what we are dealing with here with Dr. Ross in the context of this regulatory record. Thank you.

Mike.

THE SPECIAL MASTER: Okay. Thank you.

MR. RUTTINGER: Special Master, if I may add just a couple of very brief points.

You know, I heard Mr. Pennock say, and I think this really nicely summarizes the moving target that Dr. Ross's own opinions have been, that, you know, chronic tubulointerstitial nephritis is itself a chronic kidney disease. And there is a distinction here between what plaintiffs are referring to as I'll call chronic kidney disease lower case and the actual clinical condition upper case of chronic kidney

disease which Dr. Ross himself acknowledges is a distinct condition.

Plaintiff Freddy Bales was diagnosed with chronic kidney disease upper case. He was never diagnosed with chronic kidney disease lower case, chronic tubulointerstitial nephritis, acute tubulointerstitial nephritis, or any of these other kidney conditions that plaintiffs are referring to.

What it really drives back to me is that point you raised, Special Master, about saying, plaintiffs are really arguing here, you know what, that a warning should have been made about some sort of generalized renal toxicity.

Now, we are not arguing preemption today, we'll talk about that tomorrow, but I just want to preview that if that is plaintiffs' failure to warn claim, I think they are in a lot of trouble, because when the FDA reviewed all of the information out there leading up to its 2020 label change and looked at options, including options for potentially warning about chronic kidney disease, what the FDA said in response at that time was: An unqualified chronic kidney disease listing, separate and apart from interstitial nephritis, might communicate a belief in

a predictable or a generalized renal toxicity from PPIs which, if found, possibly countered clinical experience.

The last point I want to mention with respect to the methodology that Mr. Pennock said Dr. Ross employed, he said he did what he would have done at the FDA in determining that that reasonable causal association threshold was met. I see him say that that is met, I see him cite the documents that he claims meet them, but I don't see any discussion anywhere in Dr. Ross's report as to why those reports actually cross that reasonable causal association threshold.

The FDA, as you know, has a lot of different regulatory standards, including different degrees of causal association that might be relevant to, for example, a warnings or precautions indication, as opposed to adverse events. So the FDA knows that it is not just a one short hop from data to a reasonable evidence of a causal association. And that's the leap and inference that Dr. Ross makes here that we believe is so unreliable.

MR. PENNOCK: I would ask a minute to respond. Can I have one minute to respond to that?

THE SPECIAL MASTER: Yes, yes, go ahead.

MR. PENNOCK: Thank you.

First, Dr. Ross's opinions as to what the warnings should have been in '95 and 2003 are explicitly stated in his report. And secondly, to -- this -- this notion that he had to say chronic kidney disease, this capital letter thing that has just been thrown out, I think that it's -- it's belying their -- either their lack of understanding of the medicine or their attempt to just confuse the situation semantically here. It would be like telling me that there is a compound that causes atherosclerosis and there should have been a warning 20 years ago that this compound causes atherosclerosis. And they say, Well, wait a second, all of your plaintiffs suffered heart attacks that required stenting or killed them, so, I mean, what does that have to do -- they suffered myocardial infarctions. What does that have to do with atherosclerosis.

And so his -- the warning is clearly stated in his report, I think the Special Master has seen that. Thank you.

THE SPECIAL MASTER: Okay. Thank you. So I think we are going to Dr. Fine now, and who is arguing

for the defendants?

MS. RYDSTROM: That's me, Special Master, Jessica Rydstrom of Williams & Connolly.

THE SPECIAL MASTER: Okay. Hello, nice to meet you.

MS. RYDSTROM: Nice to meet you as well.

So I am -- I will try and be brief because I know I am in that coveted before-lunch spot.

THE SPECIAL MASTER: That's a bad spot to have.

MS. RYDSTROM: It really is. So I prefer to think of it as I'm batting cleanup here, right, this is the fourth, I'm batting cleanup here. But I'm not going to tread any ground that the Special Master obviously knows well about specific and general causation, and I, candidly, I don't think I need to because there is no real dispute here that they have to be separate inquiries and that the opinions that are submitted here in the Rieder case, which is the focus of this motion, have to be separately admissible.

And, of course, I would assume that there is also no dispute that plaintiffs understand that it is, of course, their burden to prove specific causation. So not just that Nexium could cause CKD

but, of course, that Nexium did cause Mr. Rieder's CKD.

And part of that inquiry is that they have to adequately address the alternative risk factors. And so where, as defendants have done here, we point to alternative causes there aren't just plausible but that are, in fact, likely and conceded, they have to put something up to show that those alternative causes weren't causation here. And I think the most -- one of the things that makes this case different is that the alternative causes that are raised and are not just hypothetical alternative causes, right, they are not just run-of-the-mill alternative causes, they are among the most common causes of CKD and -- and that's hypertension and obesity.

And honestly, Special Master, I don't think that that is fairly disputed either. So what we have here is an expert, Dr. Fine, who not only agrees, as of course he has to, that those risk factors can cause chronic kidney disease, but he goes on to say that they did contribute to Mr. Rieder's chronic kidney disease.

And the quote from his report is at Page 11 and he says, and I'm quoting here:

"More likely than not hypertension and obesity," so the hypertension from which Mr. Rieder had suffered for the vast -- the majority of his adult life, and his obesity, his swinging from overweight to obese during this period of time, that those "more likely than not contributed to his development of CKD."

So they weren't just everyday risk factors here, Special Master. They were enough that plaintiffs' own expert, Dr. Fine, thinks that it is -- that they would have given him chronic kidney disease regardless.

THE SPECIAL MASTER: Well, I think, can I ask -- can I pause you there for a minute, because, I mean, I think, you know, a lot of is made of that "it's hard to say" quote that -- that -- from I guess his deposition. And, I mean, I went and looked at that and it seems to me that what he is -- I agree with you that he is not disputing that hypertension and obesity are -- are causes of -- of his chronic kidney disease, but I think what he is saying, and unless I'm misreading it, isn't what he is saying is that the taking the Nexium precipitated the -- the development of chronic kidney disease or that it caused it to

occur sooner than it -- you know, it might have happened anyway had he not taken Nexium but it might not have happened at that time or it might have happened down the road further or something like that. And isn't that -- I mean, isn't that the kind of thing you deal with in cross-examination, the extent to which one cause versus another is more likely to be, you know, that there is multiple factors and, you know, what the role of the Nexium was is -- is something I think you can deal with on cross-examination here.

Isn't that the way to address this, instead of excluding his testimony?

MS. RYDSTROM: So, I suppose I -- a couple of things. The first is, and I agree with you, that there is a lot baked into that "it is hard to say" quote, right? And it is certainly the case that he goes on, after saying "it's hard to say," and one of the things that he clarifies, Special Master, is that it's -- he thinks that this GFR at 60, which we know is very low, he is very careful to say that it is normal for him, right. He can't, of course, say that that's a normal GFR for a man in his 40s because it's not. It is quite low. And -- and what's missing

there on this -- on this -- his attempt to sort of save the role of Nexium is whether what's normal for him is normal for others, right?

And that's the question that considers those risk factors, exactly the ones that he doesn't get to, this hypertension and the obesity. And what you are asking, really, is, is this a weight and not an admissibility question. And I think that is -- that goes back to the cases that we've cited in the brief, right, that talk about, as I know you were well aware, this really fundamental nature, gatekeeper nature, of course, that is as appropriate in the specific causation question as it is in the general causation, and I suppose the reason that it's admissibility and not weight here, why this isn't something that can be adequately addressed on cross-examination but really needs to be held out at this stage, Special Master, is because these aren't obscure risk factors that we are talking about. These are among the main risk factors for chronic kidney disease and they are the ones that he doesn't adequately address in his report or at his deposition testimony.

So when you look at the main question

here, which is: What does he leave us with, right? If it is -- if you take away, why does he tell us that hypertension and obesity are not what is actually causing chronic kidney disease, why those aren't the sole causes of Mr. Rieder's kidney disease.

And he goes back to this temporal relationship. That's really what he resorts to. And he looks at the time that Mr. Rieder was taking the medicine and he says, Well, he got worse while he was on it and he stopped getting worse when he stopped taking the medicine.

And what we know, of course, is that that temporal relationship isn't enough. It is not sufficient except in very, very rare circumstances. And, of course, this isn't the case that fits those circumstances, this isn't, you know, someone going to work in a cloud of chemicals and getting sick and then going home and feeling fine and getting sick when he shows up again for work the next day.

There are two data points in the timing. There is two data points in this analysis. The start of the medicine and the stopping of the medicine. And -- and what is not addressed here is why on that second data point, the timing of the removal of the

medicine when he goes off Nexium, what's not adequately addressed is all of the other factors that are at play, all of the other steps that Mr. Rieder is taking to improve his lifestyle, including losing that significant amount of weight.

THE SPECIAL MASTER: Yeah, I -- I hear your point here, but it seems to me, just looking at this expert, is that he does acknowledge that hypertension and obesity are also contributing factors and he puts the Nexium into the mix as well. I mean, I don't think -- you know, the fact that he doesn't conclude that those are the sole causes, I don't think that's necessarily a basis for exclusion. Again, I go back to, I think, isn't -- you know, maybe it's not the strongest causation opinion in the world, but don't you deal with that on cross-examination?

MS. RYDSTROM: Well, one thing I would say is if the question is: What is the opinion that he is giving here, right? And what is what he is trying to say? Is he saying that the Nexium caused his CKD to progress, because that's not necessarily the opinion that he articulates in his report.

In his report he says it caused it to develop, right? And the evidence that he gives for

that is really just this temporal relationship that he started taking the medicine and that his GFR declines. So that is, I could suppose, one opinion.

That is clearly unsupported because the only evidence that he gives for that is this temporal relationship, the start and the stop, and that's what we see repeatedly in these cases is not enough, right? That's what the Eleventh Circuit says in -- in Gwyn, that's what the court in Lipitor, in the Lipitor case had to deal with, this question of when you start and when you stop, if the stopping is confounded by these other things, then the expert has to do what Dr. Fine has not done here, and that is to take some effort to explain why it wasn't the obesity, why it wasn't the hypertension, and if he concedes, as he does, that those two things played a role, he has to explain to the court so that he can helpfully explain to the jury what percentage or how much of it is due to his stopping Nexium versus those other two factors, and he doesn't do that.

What he does is he admits those two other factors are at play as, of course, he has to, because they are among the two biggest factors in -- for someone developing chronic kidney disease, and he

basically says, Okay, so why wasn't it those things, well, his hypertension was treated, his obesity was mild. And what we see in those other cases, what we see in the Lipitor case, what the Eleventh Circuit told us in Gwyn is that you have to do more than hand wave at the other two -- at the other factors, you have to explain why it is that those aren't the sole cause.

And as, Special Master, as you pointed out earlier, he can't even really do that. He struggles with this, and that's what that "it is hard to say" quote is about, right. He is struggling to explain and really provides no explanation for why in the absence of his hyper -- in the absence of taking the medicine he wouldn't have gone ahead and developed that -- that chronic kidney disease in any event.

And so what we have here is -- is a question where courts who have been presented with these similar situations, what they tell us is that the experts have to do more than what Dr. Fine has done here in order for their opinions to be helpful. And that's particularly true where we aren't dealing with these obscure risk factors, we aren't dealing with having to rule out some very hypothetical risk

factor, but these are -- this is a disease that has clear and well articulated risk factors that no one, of course, not even Dr. Fine, denies were at play and they are not just any risk factors but they are among the most prominent ones, and Dr. Fine ought to have known that in order to get past causation here he needed to meaningfully engage with those risk factors and he did not.

So with that, I'll reserve the remaining time for rebuttal. I'm happy to take, of course, any questions that you might have.

THE SPECIAL MASTER: Okay. Thank you.

Okay. I'm guessing, Stephanie, are you doing this one?

MS. O'CONNOR: I am.

THE SPECIAL MASTER: Good guess, right.

MS. O'CONNOR: So I think one of the first things I want to say is I'm less interested in what the Eleventh Circuit has to say than I'm interested in what the Third Circuit has to say. And I think the Third Circuit is a lot less dogmatic, if you will, about what it is that the plaintiffs need to show. And I would point out that the Heller case relied on by the defendants actually supports that Dr. Fine did

a proper analysis, a proper differential diagnosis that rests on, I believe the expression might be "good grounds."

But let me go back a little bit, if I may, Ellen. I want to address some of the more specific issues that were raised by counsel.

First of all, Dr. Fine, as I think you know, is a board certified nephrologist. He is at the Johns Hopkins University and is most recently an associate professor of medicine there. He has been treating patients for 30 years, nephrology patients in particular, and is absolutely qualified to offer opinions here from the outset.

In terms of how he approached the differential diagnosis, he reviewed all of the records that were available to him, the same ones as the defense experts reviewed, he mapped out, very significantly, he mapped out certain parameters that he thought were key to arriving at his differential diagnosis and ruling in Nexium, ruling out other factors and ruling in certain factors as contributing. And the two facts, he ruled in PPIs definitively and he also states at Page 11 of his report that both hypertension and obesity may have played a role.

Now, counsel is completely incorrect in taking the position or stating it, she obviously didn't read Dr. Fine's report, general report or any of the other experts, for that matter, hypertension and diabetes are the main causes of chronic kidney disease, not obesity.

And by the way, at Page 11 cited by counsel of Dr. Fine's report, he indicates under this section called Obesity, which is Section B at Page 11, that:

"While it's been implicated in the development of CKD, the role of obesity in the development of CKD is somewhat controversial."

All right. Now, he doesn't say it doesn't cause it, but he says it is controversial. That is far and away from being one of the most important or one of the two most important risk factors for CKD. And, in fact, diabetes has been ruled out both by Dr. Fine as well as his treating doctor, Dr. Stoycheff.

That being said, Dr. Fine at Exhibit D of this report that we have -- can we bring up Dr. Fine's report, and I would like to go to, if I may, Special Master --

And if we go to Exhibit D, all right, and just come down.

As you can see, Special Master, Dr. Fine mapped out Mr. Rieder's weight with all of the data that he had available to him at the time starting with April 25th, 2002, when we have the first note that he started Nexium, up through March 15th of 2021, which will be the last page, all right.

And you can see as we scroll through and Dr. Fine actually describes Mr. Rieder's weight as not being really bad, that he hovers, if you will, he is on the side of obesity at times and other times not, but basically, his -- and if we can just go back a little bit, his BMI, body mass index, hovers at the 30, sometimes above -- keep going, please -- sometimes below.

So the obesity that all of the hand waving is about is at best borderline obesity, sometimes obese, sometimes not obese. And given Dr. Fine's opinion that obesity itself is controversial, this is not the level of obesity that doctors, nephrologists are worried about when looking at causes for CKD, and I believe that Dr. Fine says that.

I'd also like to talk about hypertension.

Can we go to Exhibit E of this report. And let's come down. This is a chart entitled "Blood Pressure," and, Special Master, Dr. Fine has mapped out and, therefore, considered Mr. Rieder's blood pressures beginning as early as April of 2002.

And if we can continue going down all of the way through March of 2021.

He looked at all of these blood pressures, not just two or three snippets of blood pressures that were taken out by defendants' experts, but all of the blood pressures over time. And, in fact, in his deposition, counsel may remember, he referred to Mr. Rieder's blood pressure as being beautifully controlled at times and not being that high to cause such concern. And that is throughout his deposition and in his report.

Now, contrary to what counsel says, he does rule out the two causes that he admits may have contributed, but he does rule them out as the sole cause.

And how does he do that? He does it, for hypertension, by saying: Given the patient's continuous use, PPI use, in conjunction with the patient's underlying treated hypertension, in my

opinion PPI use is the, not are, is the substantial factor in causing the development of CKD, but his hypertension may have contributed in that it was an underlying condition.

He has clearly ruled it out as the sole cause.

The same thing with obesity, after telling us in the same page, at Page 11, after indicating that it is controversial, he also goes on to say it's more likely that it associates with diabetes and hypertension and that any association of obesity of renal injury is driven by obesity's impact on these two health conditions. And, again, I remind Special Master that he does not have diabetes.

He goes on in the same paragraph to talk about: "Mr. Rieder exhibited mild obesity that tended to wax and wane at times, albeit he weighed more in an earlier period of time when he was ingesting Nexium daily."

Now, this is very key.

"The stabilization of his kidney function after his discontinuation of Nexium is more consistent with the removal of that exposure than with the effect of his weight loss. His kidney disease is currently

progressing and weight loss does have a role in slowing that progression."

Mr. Rieder's weight is not that much different today or in 2015 or earlier years when he stopped taking Nexium.

What I'd like to do is, can we put up the graph from Page -- I think it is Page 4.

In addition to mapping out all of the parameters that address Mr. Rieder's health conditions, Dr. Fine in Figure 1 entitled "Estimated GFR Changes Over Time" shows us in a pictorial form, a picture is worth a thousand words, that prior to 2006 Mr. Rieder's GFR is in the normal range. Counsel may not like that. Their experts may not like that, but Dr. Fine has opined that it was within the normal range.

And, again, I spoke to this issue earlier, CKD as an entity, and I'm not going to talk about upper or lower case, but CKD as an entity is defined as a GFR less than 60 for a period greater than three months.

In this case we do not see this decline in GFR until 2006 where it is at 51, according to the graph, and this is fully four years after Mr. Rieder

began taking Nexium.

Now, his weight is pretty much the same, his blood pressure, there are some rises, there are some dips, but if you look at this graph, what you see is a downward trajectory, clearly, of his kidney function. There are a few dips here and there and the doctors will explain that these are physiological differences, but the redline that we get to is in 2015.

Now, Mr. Rieder was taking PPIs daily and continuously until his last prescription filled in January of 2015 for 90 pills, he ingested 79 of those 90 pills, as the deposition testimony shows, which took him to the end of March of 2015.

And then what happens? We see a stabilization, as Dr. Fine pointed out, of the GFR. Blood pressure, weight, yeah, there was some weight loss, yeah, maybe he is working a little bit harder on his hypertension control. Now he is under the care of a nephrologist.

But look at that as you go across, it is very, very stable until we get to about 2020 and now we are seeing a downward decline, nothing else has changed, his weight is pretty much the same, blood

pressure is pretty much the same, but by this point in time he has advanced kidney disease.

Dr. Fine explains that aging does cause loss of nephrons, but in someone who already has CKD, and in our position induced by Nexium, that person will get to the point of no return, and, in fact, that is where Mr. Rieder is today. He is on a transplant list at age, I think 63 years old.

THE SPECIAL MASTER: How do you square this with the -- the -- the testimony where he says, you know, "it's hard to say," because, I mean, they did -- he was asked sort of the, Okay, is it your position that but for the Nexium this wouldn't have happened to him. And he says, you know, "it is hard to say." And it is a lengthy and somewhat complicated answer, but it seems to me that, you know, there is an argument that by saying, I can't -- he does say, I can't say that he wouldn't have be here if he hadn't -- he wouldn't be here today perhaps if he hadn't taken the Nexium?

MS. O'CONNOR: One thing I would say is I'm not aware that the Third Circuit is a but-for state in analysis. I believe it is a substantial factor analysis.

THE SPECIAL MASTER: Substantial factor, yeah.

MS. O'CONNOR: I would also point out, I would also point out that Dr. Fine, in his comprehensive general opinion report, which by the way is not challenged by the defendants, so Dr. Fine's opinions on general causation come in no matter what if we choose to put him on, but what he does also do in his general opinion report is he addresses not only those studies, of which there are droves of them that find a connection between PPI exposure and chronic kidney disease, chronic renal insufficiency, other forms of kidney disease, including AKI, but there are several studies that he cites here at Page 11 of his report that show that in people that already have kidney disease or at risk of it, it will actually enhance or exacerbate the progression.

So Dr. Fine has given two opinions, one that it caused the development of CKD and that it may have played a role in the progression, more likely than not played a role in the progression of his disease. It is a pretty rapid trajectory for a man this age.

THE SPECIAL MASTER: Okay. Did you want to respond, Jessica?

MS. RYDSTROM: Very briefly, Special Master.

I guess I would start where Ms. O'Connor stopped, which is, it is true, we are not challenging Dr. Fine's general causation report here, but, of course, he has to do more than the general causation report to explain why it is that, if he believes that Nexium can cause CKD, why in this case on these facts with a plaintiff, Mr. Rieder, who had this particular health history and these preexisting risk factors, Nexium actually did cause Mr. Rieder's CKD.

And that's what he hasn't done. He hasn't explained why the other two -- it wasn't the hypertension and it wasn't the obesity that caused Mr. Rieder's CKD, and that's exactly what he is doing with this quote. That is the question that he is struggling with, that is the question that he can't adequately address.

So very briefly, Special Master, if I suggested that obesity was the most common risk factor for chronic kidney disease, then I misspoke. What I -- what I -- if it is, in fact, so controversial, it's presumably not so controversial, Special Master, that Dr. Fine didn't think it was necessary to say explicitly in his report that obesity was more likely than not contributing to Mr. Rieder's development of

CKD, not the progression of his CKD, but the development of his CKD.

And that's the question that you asked me earlier, is the opinion here that these risk factors were simply making the CKD worse or is it that they in the absence of Nexium wouldn't have led to his developing CKD anyway. And the opinion that he gives us in his report is that hypertension and obesity more likely than not contributed to his development of CKD.

And what he doesn't do, Special Master, is tell us, when he says: "Given the patient's continuous PPI use," and this is in the report at Page 11, "in conjunction with the patient's underlying treated hypertension, in my opinion the PPI use is the substantial factor in causing the development of his CKD."

So what does he give us there, Special Master? He only gives us two things, that he continuously used PPI, that's the temporal relationship, right, that's collapsing the general causation and the specific causation here, and that he had an underlying treated hypertension.

And that's simply not what we see when we look at the graph that Ms. O'Connor put up. That is

not what we see when we look at Dr. Fine's own data and chart. We don't see that this person, this Mr. Rieder who had suffered from hypertension since his 30s, so since he was a young man, who was being treated with multiple medicines for hypertension and who is still experiencing the blood pressure spikes that Dr. Fine records in his chart, what we don't see it treated hypertension. We see an individual who was struggling to treat that hypertension.

And so if you take out, as the cases say that we have to, that temporal relationship, we aren't left with an explanation as to why the hypertension would not in and of itself have been enough, given his long history of this and other risk factors for Mr. Rieder to develop chronic kidney disease.

THE SPECIAL MASTER: Okay. Thank you.

So I think, happily, we are at lunch break time, and I guess what we suggested is we'd come back at 1:20. I don't know if that assumed a 12:30 conclusion or not.

Okay. All right. Well, let's -- I don't know, should we stay with the 1:20? Yeah, does that sound okay? Does that work for folks? Does anybody have a problem with that?

Okay. All right. So let's get back on at 1:20, okay.

(WHEREUPON, a recess was had from 12:32 to 1:20 p.m.)

THE SPECIAL MASTER: Let's go back on the record. And I think the first thing up on our schedule is AstraZeneca's motion for summary judgment on other grounds for Rieder.

Who is going to handle that for AZ?

Hi Mike. Go ahead, Mike Schissel.

Is he on mute?

You need to unmute yourself, Mike, I think, I'm being told.

MR. SCHISSEL: Okay. I've done it.

THE SPECIAL MASTER: There you are.

MR. SCHISSEL: Can you hear me now?

THE SPECIAL MASTER: Yeah.

MR. SCHISSEL: Nice to see you, Special Master.

THE SPECIAL MASTER: It is nice to see you too.

Okay. Go ahead.

MR. SCHISSEL: Okay. So this is our motion on summary judgment based on the issue of proximate cause and we think that the issue has been adequately briefed, but there were just a few points that we

would like to highlight for you, and I can do that, I think, in a few minutes, and I have a PowerPoint that hopefully you can see. Okay.

THE SPECIAL MASTER: Yes, I can see it.

MR. SCHISSEL: Yeah, so just a few -- just a couple of foundational issues.

Obviously the plaintiff has the burden to prove that his ingestion of Nexium was proximally caused by an inadequate warning, and if the plaintiff can prove that the label was inadequate, and we, of course, disagree that it was inadequate, we believe that it was fully adequate, but if the plaintiff bears that burden then under Ohio law there is a rebuttable presumption that the failure to adequately warn was the proximate cause for the ingestion, and then we have an opportunity to rebut it if this so-called adequate warning would have made no difference in the decision -- the physician's decision to prescribe the drug, and we can do that with unequivocal testimony from the physician that he would have prescribed the drug despite the adequate warning.

Now, there are two doctors, two prescribers in this case that matter. The first one is Dr. Konold. He was the original prescriber. He

passed away before the litigation was filed and, therefore, by no fault of either party his testimony is unavailable to us.

The plaintiff argues that Dr. Konold's death would preclude us from the ability to rebut the presumption, and, therefore, summary judgment should be denied. And what they are trying to do, effectively, if that -- if that was to occur and if that was the law, then a rebuttable presumption under Ohio law would be turned into an unrebuttable presumption merely because the prescriber happened to pass away before the litigation was filed. And we think that would be an unfair result, particularly since I don't think anybody disputes that the -- that the ultimate burden of proof on proximate causation lies with the plaintiff. And of course the plaintiff doesn't have to --

THE SPECIAL MASTER: What do you do when -- when a doctor dies with the ceding presumption?

MR. SCHISSEL: So, you know, we don't have a lot of cases in this particular situation. We've cited a number of cases in, I think it was Footnote 6 of our reply brief, where the case is made clear if the prescriber's testimony is unavailable, either somebody

decides not to take his deposition, you know, he dies during the litigation itself and his testimony is unavailable, the cases do say that at the end of the day the burden to prove causation lies with the plaintiff and, therefore, they have to prove it somehow.

And, you know, different jurisdictions can deal with it different ways, reasonable doctor or some other standard, but in no -- and we haven't found a single case, and I don't think the plaintiffs have cited a single case that said in a burden shifting situation that just because the prescriber dies it somehow turns the rebuttable presumption into an unrebuttable presumption.

THE SPECIAL MASTER: Okay.

MR. SCHISSEL: And so that's the first doctor, and that's really very much, I think, an issue for the court.

The second doctor is Dr. Wallin, and he took over the prescription from Dr. Konold effectively. He began prescribing in 2008 until sometime in 2010. His deposition was taken. The plaintiff took it first and then we examined the doctor after the plaintiff took the deposition.

And his testimony, we think, is un -- is unequivocal. He says that he thinks that Nexium is -- was a safe and effective drug, it still is a safe and effective drug, and, you know, he was examined by the plaintiff and the plaintiff obviously, you know, in the questions was suggesting that Nexium caused kidney disease. And then we asked him when we had a chance to examine him whether there is anything that he has seen or heard today that would cause him to question his decision to prescribe Nexium and he unequivocally and affirmatively said no.

And so we think that, you know, based on this record, one, they can't carry the burden on the first prescriber and the second prescriber we think we have overcome the presumption based on the deposition of the prescriber, which is what the cases allows us to do.

THE SPECIAL MASTER: Am I correct that he also testified that if there had been a warning he would have communicated that to Mr. Rieder and that Mr. Rieder testified that if warned he wouldn't have taken Nexium.

Does that -- does that change things?

MR. SCHISSEL: I don't think so because even if

we go back to the rebutting -- or the rebuttable presumption -- or rebutting the presumption, the warning, we rebut the presumption if the warning, an adequate warning would have made no difference in the physician's decision to prescribe. It doesn't say that, you know, whether or not the patient would heed any information passed on by the doctor. The question is whether the doctor would prescribe, and that would be the law -- that is the law in these learned intermediary states.

So we think that that is a little bit of a red herring or very much of a red herring in this case because what you have to focus on is whether the doctor would prescribe, and that's what the cases talk about.

THE SPECIAL MASTER: Okay. So just to be clear, if Rieder did -- if Mr. Rieder did testify that, you know, if he had been given some kind of a warning he wouldn't have taken it, you are saying that's irrelevant given the learned intermediary doctrine?

MR SCHISSEL: Yes, that's our view.

THE SPECIAL MASTER: As long as the doctor says, I still would have prescribed?

MR. SCHISSEL: That's right. That's right.

THE SPECIAL MASTER: Okay. Okay.

Sorry. Go ahead.

MR. SCHISSEL: No, and really, you know, the third doctor, Dr. Oberlander, you know, the plaintiff concedes that that testimony is -- is not necessarily something that the court has to address, because at the time that that doctor prescribed, Mr. Rieder's CKD was fairly advanced at that point. And so both sides sort of agree that, you know, that's irrelevant.

Now, if you want to consider it, you know, that testimony, too, at the end of this long -- this long back and forth, at the end of the day he says that he would still prescribe the Nexium today.

So, you know, the testimony is there, but at that point in time the plaintiff is saying, you know, you don't even have to look at that one. Really what matters is Dr. Konold and Dr. Wallin.

THE SPECIAL MASTER: Okay.

MR. SCHISSEL: And I will save anything else for rebuttal at this point.

THE SPECIAL MASTER: Thanks, Mike.

Who is talking for the plaintiffs?

MR. AUTRY: I am. Good afternoon. Pleasure to meet you.

THE SPECIAL MASTER: Nice to meet you.

MR. AUTRY: And I also wanted to thank everybody, both defense counsel and yourself, for being accommodating with my schedule a couple of weeks ago.

THE SPECIAL MASTER: No problem. My condolences on your family as well.

MR. AUTRY: I really appreciate it. It means a lot.

Going straight into the argument here on proximate causation for Mr. Rieder, I don't think it's that complicated because we are in the State of Ohio which has a rebuttable presumption that requires defendants to produce evidence, unequivocal evidence if they want summary judgment in their favor to show that a stronger warning would have made no difference in whether Rieder ingested Nexium. That evidence just doesn't exist here. And, in fact, there is substantial evidence, especially viewing the evidence in the light most favor to Rieder, taking all inferences in Rieder's favor, that a stronger warning would have made a difference.

You know, starting with the first doctor, which is several years, Dr. Konold, defendants'

position is basically that the rebuttable presumption disappears if a doctor has passed away. There is no Ohio law to support that and they are arguing for a change in the law and they should be the ones that should produce cases to say that a death of a physician eliminates their rebuttable presumption.

The Ohio Supreme Court --

THE SPECIAL MASTER: Well, would you agree with what Mr. Schissel says, that you are basically arguing that it makes a rebuttable presumption irrebuttable because obviously you can't get testimony from him, or are there other ways you are saying that it could be rebutted?

MR. AUTRY: You could potentially rebut it with the testimony of plaintiff, you could potentially rebut it with other evidence from the medical records. The -- we are not -- a physician's testimony is not the only possible way for defense counsel or a defendant to present causation evidence. There is plenty of evidence that can go to proximate causation. And the issue right now, when we are talking about what's unfair or fair, is defendants are seeking summary judgment. They are seeking judgment as a matter of law in their favor that they have met their

burden of production to overcome this rebuttable presumption.

So in the sense of fairness, we are not seeking judgment in Rieder's favor on this presumption. We are asking for a trial. And trials -- they will be able to present their evidence to a jury. We are not seeking directed verdict on this issue at this moment. We are simply saying this is a jury question, viewing the evidence in the light most favorable to Rieder and taking the inferences in his favor, and that's especially true when you factor Rieder's own testimony.

You know, the record is not silent as to what would have happened between 2003 and 2008 were there an adequate warning that -- on Nexium's label. Rieder says, If that was conveyed to me from the beginning, I would not have taken the product. If it was conveyed to me after I had started taking the product, I would have stopped taking the product. His testimony is, in fact, unequivocal, even though it does not need to be because we are the party -- we are the non-moving party on a motion for summary judgment. That's just step one.

Step two is Dr. Wallin, although you don't

have to get there because they have to rebut the presumption as to all three physicians, Dr. Wallin's testimony is that he would have discussed all medications that had a risk of kidney injury when Rieder's GFR dropped. He says that after two distinct tests and he would have wanted to know whether Rieder's medications had a risk of kidney injury.

Unfortunately for Dr. Wallin and for Mr. Rieder, defendants did not warn about even acute kidney injuries until the FDA required them to do so in December of 2014, they did not warn about tubulointerstitial nephritis until the FDA required them to do that a year and a half ago. So at this point that Dr. Wallin was meeting with Mr. Rieder, he did not have the information at his disposal in the Warnings and Precautions section to see that this medication carried a potential risk, a reasonable causal association of kidney injury to determine whether or not to take Mr. Rieder off of that.

Further, you have, again, Mr. Rieder's testimony. If this information was conveyed to me, I would have stopped taking it.

And then you have Dr. Oberlander. And, again, you don't have to get to step three because

they have to prove, they have to rebut the presumption at all three steps. But if you get to step three, Dr. Oberlander's testimony is that he had no recollection of Mr. Rieder. His testimony was before -- in November, before the FDA required -- November -- sorry -- I'm getting the years mixed up. But at the point of his testimony, he was unaware of the potential risk of long-term kidney injury and would not have associated that with Nexium even at the point of his deposition.

When he was asked to assume that Nexium could cause long-term kidney injuries, he gave a very qualified response in which he said, Well, it was a long time ago, I don't really remember Mr. Rieder. It is not the unequivocal testimony that you would need to get judgment as a matter of law in your favor as a manufacturer, viewing the evidence in the light most favorable to the plaintiff, especially -- especially where that plaintiff says, If I was told about this risk, I would have stopped taking it.

And when you go to the learned intermediary doctrine, that is important, because defendants want judgement as a matter of law that Rieder's doctors would have said, No, I am going to

prescribe this to you anyway even though you don't want it. That is not a reasonable inference, but nonetheless it would be an inference in their favor which they are not entitled to at the summary judgment stage, that Rieder's doctors would have prescribed him Nexium even if Rieder says, I didn't want to take it.

This is especially true when you consider the fact that Rieder was able to change his eating habits in 2015 so that he did not need Nexium anymore. When Rieder stopped taking Nexium in 2015 it was because he decided to change his diet, he got his heart rate under control. That could have happened in 2014, 2010 or 2006 if Rieder knew that there was a risk of Nexium.

So the idea that Rieder's doctors would have continued to prescribe him Nexium when he said he didn't want it and even if he had got his heart rate under control is an unreasonable inference and, again, defendants at this stage are not even entitled to reasonable inferences in their favor.

I need to mention a little bit this Footnote 6 that defendants reference from their reply brief. I believe it was Footnote 6. But there is a footnote in their reply brief where they cite a lot of

cases to argue that the death of a physician goes against the plaintiff.

It's important to recognize that they are citing authority outside of Ohio and they are citing cases that explicitly reject a rebuttable presumption under various states' laws. Defendants conveniently ignore that from their footnote and ignore that from their argument today.

They cite a South Carolina case that says: "South Carolina courts would not apply causation presumption." They cite a Pennsylvania Common Pleas County Court decision from 2005 that says: "Pennsylvania courts have consistently declined to apply any heeding presumption." They site an Eleventh Circuit from Georgia, that says: "Deeds," referring to a prior Eleventh Circuit case interpreting Georgia law, "forecloses a holding that Georgia law provides a rebuttable presumption that shifts the burden to the defendant."

Defendants repeatedly cite authority in their reply brief that explicitly rejects Ohio law and rejects the rebuttable presumption that we are under in this oral argument.

And I believe that is the gist of

everything I had to say, but I would be happy to answer any questions, if you have them.

THE SPECIAL MASTER: Yeah. One thing, and I don't know if it is necessarily relevant for this motion, but, you know, you've characterized what the warnings should be in a variety of different ways.

I mean, for purposes of this motion, I guess, what is it, and I guess we talked a little bit about this this morning, I don't know if you were listening --

MR. AUTRY: I was.

THE SPECIAL MASTER: -- you know, what is it that plaintiffs in the Rieder case are saying the adequate warning would have been?

MR. AUTRY: Sure. And I'm going to give a caveat because under Ohio law we are not required to draft the label language. We are required to demonstrate that the label was inadequate.

THE SPECIAL MASTER: Okay.

MR. AUTRY: But we do give several examples of adequate -- of language that would be stronger that would have, viewing the evidence in the light most favorable to Rieder, changed the course of his -- of his treatment.

So Rieder's doctors say and Rieder says that if they had even -- and this is Dr. Wallin and Rieder himself, if there was even knowledge of the risk of kidney injury at the time, that he would have stopped -- that that would have been relayed to him and he would have stopped taking it.

So to the extent the defendants are arguing that to show proximate causation we need certain magic words in the label, viewing the evidence in the light most favorable to Rieder, that is not true. If Rieder's Dr. Wallin had been aware that there was a risk of kidney injury at all and had relayed that to Rieder, Rieder is pretty unequivocal that he would have stopped taking it.

But further, if you look at our Dr. Ross, and, again, this was gone into pretty extensively this morning, it will be touched on again tomorrow in preemption because it sort of bleeds through everything, there was reasonable evidence of causal association when it comes to chronic tubulointerstitial nephritis by 2003 and acute tubulointerstitial nephritis by 1995 and at that time there was also, at '95, evidence of downstream risk that acute tubulointerstitial nephritis could lead to

chronic kidney disease, and by 2003 there was evidence of the chronic kidney disease risk.

And, again, as Paul talked about earlier, chronic kidney disease itself is a term that we ascribe to the nature of results from the tests. So chronic kidney disease is basically a diagnosis that says your GFR has been below 60 for 90 days or more, whereas a lot of the medical literature will use the term "chronic interstitial nephritis" or "chronic tubulointerstitial nephritis" instead because they are more talking about the long-term degradation or deterioration of the kidney or permanent deterioration of the kidney. But when it comes to --

THE SPECIAL MASTER: Okay.

MR. AUTRY: -- the label language itself, in Rieder's case, viewing the evidence in the light most favorable to him, there was plenty of language they could have used that would have changed the course of treatment.

THE SPECIAL MASTER: Okay. Thanks. I didn't mean to take us down a, you know, a path that may not be all that relevant to this, but I was just curious.

Mike, did you have anything else you wanted to make?

MR. SCHISSEL: Yeah, very briefly just a few points.

First of all, the rebuttable presumption is rebutted by testimony from a physician that he would have prescribed regardless of this so-called adequate warning, whatever it is, and I think we still don't know what that is in this case.

But what counsel said is that we could rebut it by the testimony of the plaintiff. Well, there is certainly no law to suggest that a plaintiff can get up and say what a doctor would have done, okay. So that's completely inadmissible testimony. It makes absolutely no sense in this case.

Secondly, counsel says, Dr. Wallin would have discussed. Well, that's not the standard. The standard in these presumption cases is would he have prescribed it. Doctors discuss adverse effects and warnings with patients all of the time, but what the relevant inquiry is, would he or she have prescribed it.

And I think in this case Dr. Wallin's testimony was pretty unequivocal. And they had an opportunity at his -- they took his deposition first. They could have said, If you had the following label

in front of you. Well, they didn't do that because, frankly, we still don't know what that label would say, but they didn't even ask that question. So what we have is the un-refuted testimony from Dr. Wallin that he thinks it is a safe and effective drug and would prescribe it today. The same testimony from Dr. Oberlander if you get there.

And, you know, I think those are the points. I mean, the key points on the presumptions you focus on, whether the doctor would have prescribed. We know with first doctor, we don't have the benefit of that, and you shouldn't change the law, which is, at the end of the day, says that the plaintiff bears the ultimate burden for proximate causation and you need to focus on the conduct of the doctor and the second doctor says and the third doctor says I would have prescribed it in any event.

THE SPECIAL MASTER: You may not have asked this at the deposition, no one may have, but was Dr. Wallin asked whether he would have still prescribed it even if the plaintiff didn't want to take it.

MR. SCHISSEL: He was not asked that at his deposition. And -- no, he was not asked that. He just said he would have passed it -- I think he said

he would have passed on the information if there was this warning that nobody can really describe to him.

MR. AUTRY: Your Honor, if I could briefly respond in less than 15 seconds?

THE SPECIAL MASTER: Fifteen seconds or less, go for it.

MR. AUTRY: Sure.

Viewing the evidence in the light most favorable to Rieder, Dr. Wallin's prescribing habits would have changed. Dr. Wallin did not know even at the time of his deposition that this was a risk of Nexium and Dr. Rieder -- Wallin did change his prescribing habits of NSAIDs because he knew at the time that this was a risk of NSAIDs.

So there was a reasonable inference in Rieder's favor that Dr. Wallin would have changed his prescribing habits and he did not testify that had the label warned of CKD or kidney disease at all that he would have prescribed it anyway. That is nowhere in the deposition.

MR. SCHISSEL: Can I respond to that in a similar amount of time?

Yeah, the cases they cite on a doctor prescribing -- changing prescribing habits is very

different from this case. It is not would you have passed on a warning or would you have discussed a warning with the patient. It is things like, in the cases they cite, the doctor says, I would have been more cautious, I would have used maybe less of a dose, I would have eased this patient up to the dose that's prescribed, that's changing a prescribing habit, not passing on information to a patient.

So I think it is a very different situation, and there is no record here that any of these prescribers would have actually changed their prescribing habits.

THE SPECIAL MASTER: Okay. Thank you very much.

MR. SCHISSEL: Thank you, I appreciate it.

THE SPECIAL MASTER: So I think we are moving on now to plaintiffs' omnibus motion to exclude experts, and I don't feel strongly about which order we want to go in. I had Mann listed first but don't feel strongly about that if folks on the plaintiffs' side want to go in some other order? Anybody?

MR. AUTRY: I think that's fine. I'm going to handle the Mann argument for us.

THE SPECIAL MASTER: Okay. I mean, is there somebody who needs to go before you? I don't think

that there is any magic to the order, but... No?

MR. AUTRY: Speak now or forever hold your peace.

THE SPECIAL MASTER: Go for it.

MR. AUTRY: Special Master, I think Mann's opinion is a series of conclusions with no methodology. Mann repeatedly praises AstraZeneca, PRAC and the FDA, although testifying in her deposition that she did not review the things that AstraZeneca, PRAC or the FDA reviewed.

So she says that AstraZeneca's submissions to PRAC were very thorough and forth going -- forthcoming, that AstraZeneca's PRAC submissions were very good. A comprehensive report by AstraZeneca. But she doesn't know what AstraZeneca had at its disposable to submit to PRAC, she doesn't know what AstraZeneca left out, she doesn't know what the clinical trials say that AstraZeneca submitted in writing.

She reviewed AstraZeneca's own PRAC submission and said they must have reviewed everything to get to this point. That is like reading a book report and grading it without reading the book. It is not a reliable expert opinion.

As an expert, you have to have -- if you are going to have an opinion about an underlying document, you should review that underlying document, and that's what Mann repeatedly needs to do but doesn't do.

She says PRAC's review was careful, that PRAC's review was comprehensive and thorough, but she did not know what PRAC considered, she did not know what the records say that PRAC considered, she did not know what the clinical trials say. She ignored the lion's share of the medical literature. She took a head-in-the-sand approach to the record and then gave opinions that PRAC, the FDA and AstraZeneca adequately and thoroughly and well summarized that record. That is not a reliable --

THE SPECIAL MASTER: Let me stop you there -- let me stop you there, because I read your papers. And a lot of your arguments, it seems to me, seem to rely mostly on her -- her supposed failure -- either the failure to identify certain missing information, and what you are -- you are saying now kind of sounds the same way, that -- I mean, you don't know what you don't know, right. And so she is presented with reports and information that were submitted to the

FDA, and if I was reading the papers, they seem to be saying that, Well, somehow she -- she didn't take into account what wasn't there.

And I wonder if that's really the right standard to evaluate testimony. I mean, you can only look at what's there and evaluate whether that's adequate or not. And, you know, in her experience as someone at FDA, can only look at a report and say, Would I have found that sufficient.

Like I say, I feel like maybe your argument is kind of saying, Well, we have to look at what's not in the report and I'm not sure that's really what experts do.

MR. AUTRY: Special Master, I believe that's an incorrect statement of what Mann did at the FDA. When Mann was at the FDA, she reviewed the medical literature, she reviewed the clinical trials, she didn't just review a one-page summary of the medical literature by a manufacturer. She didn't just review a paragraph or two-paragraph summary of the clinical trials, she reviewed the underlying data. This is not what she did at the FDA. She had a methodology at the FDA. That's a reliable methodology. That's not what she did in this case.

In this case she reviewed a manufacturer's summary of the record and then said that's a good summary of the record. She says that's a thorough summary of the record, a comprehensive summary of the record. That is not a reliable opinion of praise. In order to say that AstraZeneca did a good job in reviewing the record, you have to actually review the record yourself.

THE SPECIAL MASTER: So you are saying that she has to review all of the raw data that went into any report in order to say that that report was adequate or sufficient?

MR. AUTRY: Not necessarily all. I mean, we are not talking about --

THE SPECIAL MASTER: Where do you draw the line? Where do you draw the line?

MR. AUTRY: Daubert says that it needs to be reliable. If you completely take a head-in-the-sand approach to the record, you can't have an opinion on what that record says. She is just regurgitating AstraZeneca's opinions and saying they are her on, and not only that, saying they are good opinions.

THE SPECIAL MASTER: So I guess what I'm trying to get to, you are describing it as a completely

head-in-the-sand approach.

What is that -- what are you saying -- where is the line that what the expert needs to look at in the way of raw data, underlying data, studies that support a report and what, you know, obviously they can't review every piece of data that goes into every report, and that's not what FDA reviewers do, but where -- where is the line, that's what I'm trying to understand.

MR. AUTRY: Well, when it comes to medical literature, we've identified about, I think, three dozen relevant pieces of published peer-reviewed literature. That's not an insurmountable burden to review those, but we would not be here and we would not be filing a challenge to her if she reviewed 30 out of 32, but that's not what she did. She reviewed a summation of the medical literature and then said that's a good summation. You just can't -- that's not a reliable opinion if you don't look at the underlying record being summarized.

This is not -- our Daubert is not against her because she should have spent 10,000 hours as opposed to 2,000 hours. You know, we are not going down that road. Her opinion is completely unsupported

and she is a mouthpiece for AstraZeneca to say -- I mean, like, look at her opinion that AstraZeneca appropriately labeled Nexium at all times. I cannot for the life of me determine how she reaches the conclusion that AstraZeneca could not have warned about acute interstitial nephritis before 2014. I have no idea how she gets there. I have read her report several times, I have read her deposition several times. How does she reach the opinion that in 2013 AstraZeneca's label was appropriate? How does she reach the opinion in 2002 that AstraZeneca's label was appropriate? I'm clueless. And I've read her report several times and I've read her deposition several times.

You need a methodology to get from Point A to Point B. Your methodology cannot simply be the manufacturer said it so I agree. That's just not a reliable opinion under Daubert. The manufacturer can say it to the jury just without an expert hired to say the same thing and say we did a good job. And if the manufacturer -- and if the expert is going to say we did a good job, the expert needs to review the same thing you were reviewing as the manufacturer to come to the conclusion that your summary was a reasonable

one.

I mean, she says it was correct, thoughtful, extensive, comprehensive and careful. I don't know how she is reaching those opinions without reviewing the underlying literature. She is just rubber stamping assessments without reviewing those assessments. Again, it is like saying a book report is good without reading the book and this is not what she did at the FDA.

THE SPECIAL MASTER: Okay. Let me ask you: Can she -- do you think she can testify as to what -- whether the process that FDA followed in certain circumstances was appropriate?

MR. AUTRY: I think her FDA opinions suffer the same flaw as her AstraZeneca and PRAC opinions. She did not look at the underlying data to determine what was being considered or not considered. So I don't think she can give a reliable opinion that the FDA thoroughly reviewed what was out there because she didn't and she didn't try to. Like, how can you give an opinion that the FDA conducted a thorough review if you don't even attempt as an expert to conduct a thorough review yourself. I mean, it is not like she made an effort and failed, it is not like she made an

effort and fell short, she just didn't try to conduct a thorough review herself. She just jumped straight to the conclusion that PRAC, the FDA and AstraZeneca conducted a thorough review.

THE SPECIAL MASTER: All right. Anything else?

MR. AUTRY: I believe that's it, your Honor.

THE SPECIAL MASTER: Okay. Thanks. Who is going to respond?

MR. MILLER: I'll respond to those.

Can you hear me okay, Special Master Reisman?

THE SPECIAL MASTER: I can. Nice to meet you.

MR. MILLER: And for the record, I am Jake Miller on behalf of AstraZeneca.

So there's a few things I'd like to say in response to Mr. Autry's presentation. The first is he did not even mention, from what I could tell, anything related to the first two arguments that are actually made in their briefing. So I will take from that that plaintiffs have conceded that those two arguments have been adequately and fully addressed and that they are appearing to now shift the focus of their arguments.

For Mr. Autry's presentation, you might be led to believe that Dr. Mann is somehow being put up

as an expert whose sole job is to opine on PRAC issues. And I just want to point out some context, right. Dr. Mann is offering a regulatory opinion about the appropriateness of FDA's decisions vis-à-vis the content of the Nexium label when it comes to kidney disease. PRAC is one piece of the data that goes into that analysis, it is just that, a piece of data. And I'm going to talk about that but I just want to make sure that we are talking about the correct context. You know, Mr. Autry's presentation seems to suggest or leave the listener with the view that this is somehow an auditing opinion or something, which it is not, it is a regulatory opinion.

Now, Mr. Autry said a couple of times that Dr. Mann is simply regurgitating opinions or rubber stamping opinions without doing her own analysis. Frankly, Special Master Reisman, this is an absurd position. I'm going to start just by talking about the FDA side of things and then I'll go into the PRAC.

Mr. Autry said that Dr. Mann essentially didn't do any of her own homework, so to speak, failed to review any of the relevant underlying information and simply just regurgitates what FDA concluded, and that is a gross, gross misrepresentation of the record

here.

So just as an example, if you look at both Dr. Mann's written report and importantly her materials considered list, it is littered, littered with the leading studies discusses a potential association between PPIs and kidney disease, the very studies that form the basis of FDA's own analysis. She reviewed the Lazarus study, which is MCL No. 103; she reviewed both the Xie studies, which is MCL Nos. 160 and 161; she reviewed the Attwood publication, which is MCL No. 14, which discusses the randomized Zofran and Lotus studies; she reviewed the Moayyedi publication, which discusses the randomized COMPASS study. And I don't mean to just make this a long list of things that she reviewed, but just because I think this was the focus of plaintiffs' presentation here, she reviewed Simpson, MCL No. 153; Tomlinson, MCL No. 157; Wu, MCL No. 159; Antoniou, MCL No. 1; Arora MCL No. 3.

Special Master Reisman, I can go on and on and on. I don't want to belabor the point. What I want to suggest to you -- well, not suggest. What I want to affirmatively say is Mr. Autry's assertion that Dr. Mann essentially didn't do any of her

homework and didn't review any of the underlying studies herself is simply a misrepresentation of the record and the report.

Now, in addition --

THE SPECIAL MASTER: How do you respond -- hold on.

How do you respond to plaintiffs' claim that -- where -- that she reached conclusions without supporting documentation for, I think some examples that I saw were the PRAC submission and data relevant to FDA's 2020 conclusion, and I think her deposition testimony was cited by plaintiffs with regard to those as areas where she did not -- or she said she did not review support documentation.

Do you agree with them, disagree?

MR. MILLER: I don't agree with plaintiffs' characterization at all. So there was a few -- there were a few things that you flagged there, Special Master Reisman. I'll try to address them all. If I forget one, please remind me to address it.

But you mentioned, for example, the FDA 2020 decision. So, you know, I started my presentation by talking about all of the underlying studies that she herself reviewed, not just FDA's

analyses but the actual studies themselves, and those leading studies are the very things that FDA itself was -- was primarily and principally focused on in its sort of 2016 to 2020 timeframe in evaluating whether there needed to be a label update in 2020.

Now, in addition to reviewing those studies, Special Master Reisman, Dr. Mann also reviewed internal FDA analyses themselves, right. She reviewed, for example, the FDA's internal analyses of the Lazarus study, of the Xie study, of the Antoniou study. She reviewed FDA's 2018 mechanism paper by Dr. Fanti, which by the way notes that FDA had and considered the PRAC analysis, which I'll get to. And, I mean, again, not to belabor the point, Special Master Reisman, but Dr. Mann reviewed copious materials demonstrating FDA's analysis of the kidney safety issues over many, many years. Just as an example, Item No. 66 on Dr. Mann's materials considered list consists of more than 500 pages of internal FDA analysis of renal safety issues spanning many, many, many years. And Dr. Mann's written report, which Mr. Autry gives very short shrift to, fully discusses the careful and thorough FDA analysis, again, over many, many, many years. I mean, we are

talking going back to, you know, the mid-'90s all of the way up through 2020, the FDA performed numerous internal analyses of these issues. And the materials that Dr. Mann reviewed clearly, clearly gives her an adequate basis to say that the FDA was appropriately and carefully assessing these issues and going over them.

Now, Special Master Reisman, I believe your question all touched on PRAC, and, okay, so let me address that now.

You know, Mr. Autry, I think, really ignores the scope of the information that is available from the documents that Dr. Mann herself reviewed. And I think it is important to mention those because, again, plaintiffs would have you believe that what happened is something completely different than what actually happened.

Now, Dr. Mann's report includes an in-depth discussion of PRAC's CKD assessment, the accuracy of which plaintiffs do not and cannot dispute. And the PRAC materials that Dr. Mann reviewed established the following undisputed facts, I want to underscore that point, Special Master Reisman.

Now, first, PRAC's review was prompted by

the publication of the Lazarus and Xie articles in 2016, again, both of which Dr. Mann reviewed and discussed in her report. The information that Dr. Mann reviewed establishes that AstraZeneca submitted renal safety data to PRAC on more than ten thousand patients and identified in that the number of renal events observed in that universe of patients.

Now, the information that Dr. Mann reviewed also shows that in addition to AstraZeneca, Takeda and Eisai also submitted renal safety data to PRAC. And in reaching its conclusion, PRAC, this is PRAC now talking, said that this is the information that we reviewed. And this can be found in the final PRAC report. I believe it is on Page 22 in Section 3.2.

PRAC says across all submissions for all PPIs 64 trials, 64 trials, including over two -- excuse me -- containing over 22,000 patients were included. They say 14 of these trials were more than a year long and they included over 3400 patients and four trials -- of those, four were more than three years in length or three years or longer and included over 1100 patients.

And PRAC went on to explain, Special

Master Reisman, that these trial timeframes are more than sufficient to reach conclusions here because the Xie study, which is one of the two studies that caused PRAC to look into this, said that -- or showed that the peak in the relative risk of renal outcomes, including CKD, occurred after one to two years of cumulative exposure.

So it was only after assessing all of this data that PRAC reached its conclusion. And this universe of information, again, all of which Dr. Mann had available to her and considered, it plainly and clearly provides sufficient grounds for Dr. Mann to offer her opinion here.

And, again, I want to underscore plaintiffs do not and cannot dispute the accuracy of the PRAC discussion in Dr. Mann's written report. Instead, you know, what they've done, Special Master Reisman, is they've sort of pivoted to this theory that plaintiffs have about AstraZeneca purportedly, you know, manipulating is the word they used, manipulating the data, and, you know, they claimed that essentially, as I understand it, it is tough to fully understand the argument, but as I understand it, they are basically saying that in order for Dr. Mann

to be able to offer any opinion at all, she has to essentially effectively audit AstraZeneca's submission in order to affirmatively rebut plaintiffs' manipulation theory, for which, again, there is no evidence or basis in the record.

And I just want to emphasize one or two other quick things, Special Master Reisman, with respect to this. The materials that Dr. Mann reviewed make clear that AstraZeneca enumerated the selection criteria it was using to identify responsive information to PRAC's request, and it is undisputed, undisputed that PRAC has never raised concerns with AstraZeneca's submission or AstraZeneca's selection criteria.

And Dr. Mann also made clear in her testimony that it is common for companies in response to broad requests for data like it to identify a universe of data in responding and that is precisely what occurred here. I hope that was responsive to the Special Master's question.

THE SPECIAL MASTER: Yes. Thank you.

MR. AUTRY: Your Honor, if I could briefly respond?

THE SPECIAL MASTER: I kind of thought you

might.

MR. AUTRY: Thank you.

Your Honor, I have no idea what AstraZeneca's counsel is talking about when he says that Dr. Mann reviewed the clinical trial data because she explicitly says in her deposition she did not. You know, on Page 300 of her deposition:

"I looked at the summary of those trials.

"Okay. You looked at the discussion of those trials in AstraZeneca's submission to PRAC?

"Correct, along with PRAC's review as well as their assessment of those data."

She did not look at the data. I don't care what's on her clinical trials list. She testified under -- or what's on her materials considered list. She testified under oath as to what she considered and what she didn't. And under oath she said she did not look at the clinical trial data.

Now, even though she didn't look at the clinical trial data, her report in her deposition is full of opinions about what the clinical trial data shows or does not show.

"In clinical trials no significant imbalances were observed for renal function and no

cases of interstitial nephritis were observed."

She did not look at the data to reach that conclusion. She looked at what AstraZeneca said about the data to reach that conclusion.

"No cases of interstitial nephritis have been observed in clinical trials."

She did not look at the clinical trials to reach that opinion about what the clinical trials showed. She looked at AstraZeneca's summary of the clinical trials to reach that opinion about what is in the clinical trials. That is not a reliable opinion.

THE SPECIAL MASTER: Hold on. I just want to ask -- I just want to ask you a question.

When you talk about clinical trial data, are you talking about raw patient-by-patient data? What exactly? I'm just trying to understand what the documents are that you think she really did need to review.

MR. AUTRY: Okay. So there are -- when you have a clinical trial there is obviously thousands of potential pages to review. All she reviewed was what AstraZeneca put in as their summary to PRAC of what those clinical trials show. She did not go even one step beneath that. And then she looked at what PRAC

responded to AstraZeneca in their letter response. These are summaries of summaries of summaries that -- and she is just taking them not only as face value. She is saying they thoroughly, accurately and correctly summarized the level beneath them. That is an unreliable opinion because she is not looking at the level beneath them. She looked at the summary.

THE SPECIAL MASTER: And the level beneath it is what? It's the actual patient data?

MR. AUTRY: Yes. And she is not even looking at how many trials were conducted. Like she is not even going a level above that, right. So a level above that and still relatively surface level would be how many trials AstraZeneca conducted to determine if AstraZeneca included all pertinent trials. She is giving an opinion that AstraZeneca included all pertinent trials, but she does not know how many trials AstraZeneca had. She is giving an opinion that AstraZeneca accurately summarized the trials but she did not know what AstraZeneca was looking at to reach those summaries.

And, you know, defense counsel is saying that this is unreasonable to expert their expert to audit their conduct. But that's the opinion their

expert is giving. Their expert is giving an audit opinion that I've looked at what they did and they did good. That has to be a reliable opinion.

THE SPECIAL MASTER: Thank you.

All right. I think we can move onto the next one. I think it's -- the next one on my list was Dr. Deo.

Hi. Jessica, are you going to do that one?

MS. RYDSTROM: I am not, your Honor, because I am opposing it.

THE SPECIAL MASTER: Oh, sorry.

MS. RYDSTROM: So I would rest, but I don't think -- I don't know if that would go over very well.

THE SPECIAL MASTER: I don't think so.

MR. PENNOCK: Everyone will be able to rest pretty quickly because my argument will be very short, Special Master.

THE SPECIAL MASTER: Okay, Paul.

MR. PENNOCK: You know, the papers lay it out I think pretty clearly and I think it boils down to this: If Dr. Deo wants to come to trial or I should say if his lawyers intend to try to put him on the stand to say that the causes, the only causes of the

chronic kidney disease in Mr. Rieder are the things that he outlines, he can't do it. He should be excluded. He should be precluded from offering that view, that opinion because what -- because he didn't rule in everything that he needed to rule in and then rule them out. This is sort of basic Daubert analysis by any expert giving a causation opinion about anything, whether it's a defense expert or a plaintiff expert. You have to rule things in. You can then rule them out.

You can say: Yes, I considered PPIs? And do you think that that played any role in contributing to his disease? No. Why not? I reviewed all of the literature, I reviewed everything that is out there, et cetera, et cetera, and I don't find that there is sufficient support that these drugs can actually cause chronic kidney disease and, therefore, I ruled it out. That's how he would do this.

THE SPECIAL MASTER: So, Paul, is it your position that Deo has to offer an opinion on whether PPIs contributed or not in order to testify at all?

MR. PENNOCK: No, and I was about to give that up, Special Master.

THE SPECIAL MASTER: Okay.

MR. PENNOCK: He could take the stand and he could take the stand to say, Look, I have reviewed his medical history and I believe that, you know, this -- his cardiac issues were a substantial factor in the development of his disease and whatever else he wants to throw in the mix. I think there are a couple of other things in the mix. He said, I think those contributed to his disease. But, you know, have at it. I mean, if he --

THE SPECIAL MASTER: So, I mean, you were anticipating my question. Doesn't that just go to the usefulness of his testimony to the jury, right?

MR. PENNOCK: Yeah, then I think it's like, okay, that's good. And what about PPIs? I don't have any opinion on that. Why not? Because you didn't read anything or review anything. Nothing. I mean, I almost would invite him to give that opinion, but -- you know, to come to the stand for that.

But the bottom line is, I think certainly if we put -- and they said this in their papers, and I don't really disagree, if we put up the cardiologist and say, Look, I looked at all of the cardiology here and I really don't think that his cardiac issues were substance or significant, and I don't think that they

in a meaningful way contributed to this kidney disease and here is why. Well, then they can put Deo up and I can't attest that, to say, Look, I looked at all of the cardiology stuff too and I do think it contributed. That's all fair game.

THE SPECIAL MASTER: So this is -- Rinder is the expert you are talking about, right?

MR. PENNOCK: Yes.

THE SPECIAL MASTER: And so, I mean, I think, you know, as reading over this stuff, it seems to us that the scope of his testimony is going to depend on what -- if Rinder testifies what he says, right?

MR. PENNOCK: I think that's exactly right. And that's why he could end up getting on the stand. But they are going to have -- they will have to be very careful and circumscribe because they can't lead, either deliberately give testimony or leave the impression that he is giving an opinion that these are the only causes of his chronic kidney disease, because if they do that, then he is clearly opening himself up to the cross of, like, Well, you don't have any idea because you didn't even consider all of this stuff that the jury now knows. The jury now knows more than you know about PPIs and chronic kidney disease because

they've actually heard it and you didn't.

So I think we are on the same page, Special Master, and maybe I am with the defendants as well. I mean, sometimes with all of this briefing, as you pointed out several times, we might be missing each other, but that's where plaintiffs stand on Deo.

Thank you, Special Master.

THE SPECIAL MASTER: Thanks, Paul.

MS. RYDSTROM: I will be similarly brief, Special Master.

I mean, from the amount of times that Mr. Pennock mentioned cross-examination, I think we are in heated agreement that that is the place to address any deficiencies in Dr. Deo's opinion. And, look, certainly if Rinder is in, he is in. There is absolutely no question about that. But he comes in regardless of Rinder because he actually has opinions that are -- exist separate and apart from the responsive agreements to Dr. Rinder, and those are, of course, that hypertension, the issue or the sort of disease with which he is so intimately familiar, is the likely cause of Mr. Rieder's CKD.

And separately, taking on two issues that Dr. -- that Dr. Rinder -- I'm sorry, the Rinder/Rieder

thing is really going to trip me up here, so I'll have to go a little bit slow. Two issues that Dr. Rinder raises in his report, Dr. Rinder says that Mr. Rieder's blood pressure was well controlled, right, that's obviously a very hotly contested issue in the litigation. It came up when I was talking to you about Dr. Fine, it comes up here. It is really the key risk factor that we believe explains Dr. -- Mr. Rieder's development of chronic kidney disease, and there is going to be a lot of discussion about that.

THE SPECIAL MASTER: Yeah, but to go back, to go back to -- and I'm glad you mentioned Dr. Fine, because I think in a lot of ways this is a mirror image of the argument we had on that. I mean, how -- how can Dr. Deo really address ultimate causation without taking a potentially relevant alternative cause into consideration? I think, and I think similar issues, as you will remember, came up in our discussion of -- of Dr. Fine. So, I mean, I think these two are kind of related.

MS. RYDSTROM: So here is the difference. The difference, Special Master, is that we don't have the burden of proving causation, right. We don't ever

have that burden, and that burden always remains with plaintiffs. And so what the cases say, and this is true about the Third Circuit cases that are cited here by plaintiffs with respect to Dr. Deo, all they say is that once defendants, right, in a case of plaintiffs who have that burden, once defendants have raised some alternative cause, that the burden shifts back to plaintiffs, right. And that's all those cases say. There are no cases that are cited by the plaintiffs here that talk about what happened when -- what happens when the defense expert does or does not pass an opinion on the agent at issue. And that makes sense, right, because that -- that burden shifting is one that is uniquely applicable to plaintiffs. And the only case that we found that's cited by either side that talks about our situation, right, where the defense expert has an opinion that is -- that specifically, and this is not a secret, right, he is open about it, that specifically is not passing an opinion on whether the medicine specifically caused the injury in this particular case is that Burton case from the -- from Wisconsin. And that case essentially says it's fine for a defense expert.

THE SPECIAL MASTER: What is the case relying on

for that proposition?

MS. RYDSTROM: It is the Burton vs. American Cyanamid case. It is cited in the papers. It is from the Eastern District of Wisconsin. And, of course, I expect that I'm going to hear in just a minute from Mr. Pennock that -- that that is not a Third Circuit case. Concededly, it is not. Wisconsin is very far from the Third Circuit, I agree. But I would also note that there is no cases cited by plaintiffs that specifically say in our situation, right, a defendant has to consider even all of the agent that's at issue in the case.

And, of course, that makes sense for a couple of reasons. One, because most defense experts are going to say general causation is not there, right. That's not this situation because Mr. -- Dr. Deo is not -- is not offering that opinion, but it also is because most plaintiff experts, unlike this case, right, most plaintiff experts don't try to -- to avoid giving an opinion about whether or not a particular agent has caused the -- the disease or the injury in this case. So it's actually you could see in that respect not something that might come up all that often.

Now, here, of course, Dr. Rinder doesn't himself offer that opinion, that PPIs were specifically the cause. So that opinion that Dr. Deo gives that it was hypertension that caused it is absolutely in, whether or not Dr. Rinder ever shows up at trial or not. And -- and that opinion is -- is separately admissible.

That's the issue here. It's not purely a responsive opinion, although, of course, it is, and I have no doubt that Mr. Pennock at trial is going to do exactly the cross-examination that he just did of Dr. Deo. Well, Dr. Deo, you know, what are you doing here if you are not giving an ultimate opinion. And the jury may or may not weigh that as against all the other information and all the other opinions that Dr. Deo offers about the interplay of Mr. Rieder's underlying CV disease, his longstanding hypertension, and the kidney disease that he ultimately developed.

MR. PENNOCK: May I reply, Special Master?

THE SPECIAL MASTER: Sure.

MR. PENNOCK: First, I just want to be clear, I guess I haven't been, I am not suggesting that Dr. Deo has to give an ultimate opinion on his evaluation of the contribution of PPIs to the disease here. He

could dispose of it by, as I would have expected, by reviewing all of the general literature and then the defense expert comes in and says, I ruled it out because I don't think that it can cause chronic kidney disease. So I did not have to incorporate it in my analysis of the individual factors that were involved in this -- this person's disease because I don't think he can do it.

So, but, again, I will say that other than that Eastern District of Wisconsin case, there is -- we agree, there is no case law we can find where going the other way or the way that that Eastern District case went, which is you can put an expert on the stand to testify to what caused something without ruling in everything and then ruling out those things that have to be ruled out.

Now, I do think it is different than the Fine situation. I think the Fine situation they are trying to parse out this issue with Dr. Fine that I think was addressed, but I don't want to start restating or getting into Stephanie's argument. Thank you.

THE SPECIAL MASTER: Okay. Thank you. I think that's it on that one.

The next one I have is Palese, P-a-l-e-s-e.

MS. MARTINES: Dr. Palese.

THE SPECIAL MASTER: Hi, Buffy.

MS. MARTINES: Good afternoon, Special Master. This is Buffy Martines on behalf of plaintiffs, and I'm going to argue the motion to exclude Dr. Palese.

I took Dr. Palese's deposition last summer, and the truth of the matter is she is quite a puzzle to me. She is not qualified to give her opinions and her methodology is not reliable, so I'm not sure exactly what she offers, but let me take each of those piece by piece if I can.

She is not -- Dr. Palese is a gastroenterologist. She is not a nephrologist. She is not even a primary care physician for kidney patients. She has no experience evaluating patients with CKD to determine if PPI is a cause. During her deposition she conceded to me that she often works in one of these cross-functional teams where nephrologists are used for -- for patients with kidney disease. So I'm not exactly sure why she was selected for this, other than she is a big fan of PPIs, big fan.

The defendants response to that is you don't need to be the best qualified expert to testify. I agree with that. I think that's what the case law says, but you've got to be kind of qualified. You don't just get to pull anybody out and say, This is pretty close, so we are going to put her up.

In support of her qualifications, the defendants also say she routinely treats patients with multiple comorbidities, including kidney disease, and she is comfortable doing that. Again, not the standard to qualify an expert. I'm glad she is comfortable treating these patients. I hope they are comfortable with her, but, again, that doesn't qualify her to take the stand and testify as an expert in this litigation.

Now, even if for some reason that you are to determine that she is qualified, in the second prong of this analysis, her opinions are not reliable. And let me just kind of walk you through my experience and what I gleaned from Dr. Palese during her deposition.

Her big opinion is that Mr. Rieder's CKD was preexisting to the time he took the PPIs. She says that on Page 17 of her expert report. During her

deposition she said she knows this because she did some calculations. I asked her about those calculations and she couldn't tell me a whole lot about -- I asked if she had documentation of the calculations, and she said no, she did it on a website. I asked her what website she used and she didn't remember. She said she had to Google it. When I pressed her on that and continued to ask her about documentation or the name of the website or any detail about this calculation, she told me it doesn't matter, she just knows.

Take that a step further. The lab report that she relies on to make these mystery calculations don't show CKD. And earlier this afternoon in your -- when we were talking you mentioned in another argument, you said you don't know what you don't know, and I've heard you say that before, and I'd add on in the case of Dr. Palese, we are never going to find out. We are never going to find out what we don't know. We are never going to be able to test these calculations or how she got to where she got.

During her deposition she repeatedly stated that as part of these calculations she needed to use his age, Mr. Rieder's age, and she said over

and over again that he was 30 years old. Over and over again. Finally, I pushed her on that and asked her what his birth date was and asked her to do the math and she conceded that he was 44. But she said that mistake didn't matter either. Well, we don't know if it mattered or not because we don't have the calculations.

So I'm just not sure how reliable it is and how we can possibly depend on her analysis in support of this opinion. She -- you know, she says that she did these calculations and that for a 44-year-old man the GFR shows that he has CKD. I guess we are just going to have to take her word for it because there is certainly no paper to back that up. In fact, when plaintiffs counsel went back and actually did the math with the one website she could remember, not that she could confirm that she used, but that she can remember, when plaintiffs counsel went back and did the math, the GFR was fine.

So when you add all of this up, Dr. Palese has no business testifying in front of a jury.

Now, in their brief I believe defense counsel said in different pieces, Well, she briefly misspoke. Well, it is just like when you switch

Fahrenheit to Celsius. Well, it is just like this.

I don't disagree that if you took any one of these components and looked at them in a vacuum, maybe it's just an honest mistake, maybe you just briefly misspoke, maybe it is common sense, but not when you take them all together. You can't look at each little piece in a vacuum and say, That's okay. You look at it all together.

And you have an expert that's not qualified, she is not a nephrologist, she is not even close to a nephrologist. She doesn't analyze CKD and determine causation. And her methodology, she can't even remember how she came to the conclusion she came to. And for these reasons we would ask that she be excluded, and I would like to reserve the rest of my time for rebuttal.

THE SPECIAL MASTER: That's fine.

Jessica?

MS. RYDSTROM: Thanks, Special Master. So let me tell you why Ms. Martines raised the question why is she here. Let me tell you why she is here.

Dr. Palese is here because she is clearly qualified to determine what caused Mr. Rieder's CKD. She is a gastroenterologist, she is here in town at

Georgetown Hospital, her -- she is as terrifyingly credentialed as most of the rest of these folks, right. She -- she teaches at Georgetown Medical School, she went to Mt. Sinai School of Medicine, did an internship and a residency at Georgetown, and her -- her specialty there, your Honor, and her former board certification was in internal medicine, right. That is exactly the type of training that she received. She now specializes in gastroenterology.

Now, what she said and what I think I heard in the briefs was that Dr. Palese is somehow not qualified to know whether PPIs caused -- caused Mr. Rieder's CKD, and that's not what Dr. Palese said at all. What she said is that of course, as one would hope any treating doctor would do, and that's one of the main distinguishing characteristics of Dr. Palese here, is that she is seeing patients all of the time like Mr. Rieder, right, and she may not be seeing them for their chronic kidney disease. That is not the disease state that she is treating, but she is treating them for things like what Mr. Rieder had, which is GERD, right, the kinds of diseases that cause people to start taking medicines like PPIs.

And what she said, of course, was what you

would expect any doctor to do, which is all patients should be evaluated for all causes of their kidney disease or other diseases and if she needed help in a particular case or a particular consult, she would bring that in.

THE SPECIAL MASTER: Can I stop you for a minute?

MS. RYDSTROM: Sure.

THE SPECIAL MASTER: Leaving aside her qualifications for a minute and, you know, I think the crux of her testimony is supposed to be that his chronic kidney disease was preexisting to his taking Nexium. And the basis, as I'm understanding it, the basis for that conclusion is a calculation, a GFR calculation. And I think what I'm understanding from the papers and what Ms. Martines says, no one can, as we sit here today, know exactly what numbers she put into that calculation, right.

And so if his, as I understand the science, if the GFR is 60 or less, that's -- that's an indicator that he has got chronic kidney disease. And I guess the question I have for you is: If she puts the right numbers in, you know, the -- I think creatinine goes into it, I think age goes into it. I

don't know what else goes into it. But if she puts the right numbers in, does she still come out with the same conclusion?

MS. RYDSTROM: Well, here is what -- we know what it's based on, right, we know what she put in because she says it was based on the fact that his creatinine was 1.4 and we know from her report that she had his date of birth, right? So those are inputs.

And Ms. Martines is right, she cannot remember the website that she -- that she -- to which she inputted, but what she says is that for, in her experience and, right, so combining her experience and with the calculations that she did, it results in an eGFR of 60. And I should stop myself here --

THE SPECIAL MASTER: Let me stop you.

How does experience come into this?

MS. RYDSTROM: Because what she says --

(Indiscernible due to simultaneous talking.)

THE SPECIAL MASTER: -- doing the calculation?

MS. RYDSTROM: That is the Fahrenheit to Celsius is that Dr. Palese says is, Look, I see patients like this and I have a sense, right, given my clinical

experience that when you have a creatinine of 1.4 and you are roughly in, you know, a certain age group, that she believes that gives you a -- that she would know what someone's eGFR is.

But I'm going to stop right here because it's not actually just Dr. Palese that says it. Dr. Fine, you'll remember Ms. O'Connor put up the chart, right, you'll remember Dr. Fine's chart with the zigzags that she put up that show his eGFR and lo and behold, right, at around the same time as we get that 1.4 creatinine reading, Dr. Fine lists on his chart an eGFR of 61.

So -- so here -- I guess I am surprised at how hotly we are disputing two experts on opposing sides who fundamentally come up with a very similar number. And I guess what I would say is all of this question, if we are talking about testability, they tested it, right. The reply that was submitted to the Special Master reproduced the plaintiffs' -- what the plaintiffs got, the different number that they got when they say they inputted into one of the websites that Dr. Palese potentially used, they put in those inputs and they got a different number.

And that, your Honor, is a

cross-examination. I mean, presumably that's an issue for cross. They tested it. It was a testable methodology, right. They attempted to recreate it and they got a different number.

THE SPECIAL MASTER: But they don't know they are using the same formula or the same calculator, right?

MS. RYDSTROM: And presumably, Special Master, that's an issue for the cross-examination as well. I mean, there is a lot of stern -- wrong about this, you know, this misstatement. And I read the transcript and, I mean, Lord help us all, as Ms. O'Connor pointed out earlier, I may have misspoken and I was talking for only 20 minutes. After five hours or however many hours of her deposition, Dr. Palese said, and I looked at it, and she -- she didn't say it just once, concededly, she said it and five pages later she fixed it, right. She fixed his age and -- and counsel, Ms. Martines, had the opportunity to ask her whether or not that error changed her opinion, had every opportunity to interrogate whether that misstatement, right, what she believed at the time and whether she believed he was in his 40s or whether she -- she believed he was in his 30s, that -- that was the time

to explore those, and I believe that Ms. Martines did.

And so what Dr. Palese answered about the work that she did, the calculations that she did, whether she could remember those calculations, those are all those are all potential fodder for cross-examination.

And ultimately, when you look at it, the numbers that she came out with are not all that dissimilar from what Dr. Fine concludes and puts in his chart.

MS. MARTINES: May I respond, Special Master?

THE SPECIAL MASTER: Yes.

MS. MARTINES: I wrote down a few things that defense counsel said. She is clearly qualified and a list of all of the great places that she went to school and she worked at. At the end of the day that's great. She did go to some really high-end schools and worked at some great hospitals. And I'm sure she is a fine gastroenterologist. She is not a nephrologist. She is not qualified to determine causation.

And by the way, on Page 17 of her report, that's exactly what she tries to do, and I'm reading a direct quote:

"In contrast, there is no evidence that Nexium caused or substantially contributed to Mr. Rieder's CKD."

That's exactly what she is trying to do in this report and she is not qualified to do it.

Defense counsel said we know what she put in the calculator. No, we don't. No, we don't. She said multiple times that Mr. Rieder was 30 years old when I corrected her, not when she corrected herself, when I corrected her. She said, Oh, I meant 44. And I said, Which number did you put in the calculator? And she said, I put in 44.

We don't know that for sure. She corrected herself. We are never going to know what she put in that calculator because she didn't keep any documentation of it.

Defense counsel said that kidney.org is the website she potentially used. Again, we are never going to know which one she used because she didn't document it.

These are things that an expert in litigation has to do. Maybe if we are treating patients we can do things a little bit different. Maybe when we are treating patients you can rely on

your sense of what's going on, but there are rules in litigation.

Daubert and its progeny laid out specific requirements, and I have a right to depend on that those specific requirements are met when an expert takes the stand. It's not a matter for cross-examination. Daubert is a gatekeeping function. If Dr. Palese can't meet the basic requirements to get through the gate, it is not a cross-examination issue. It is a she doesn't come to trial issue. She hasn't met those qualifications.

With regard to whether or not we've been able to test her hypotheses, we got as close as we could without knowing the specific age she used and the specific website she used, and you know what happened. The results were different than what she said happened. For those reasons we do believe that Dr. Palese should be excluded.

MS. RYDSTROM: Two points, Special Master.

The first is of course we allow experts to testify based on their clinical experience and their experience treating patients all of the time. We absolutely do that. Many, many an expert comes to trial and testifies just as Dr. Palese did about

things that they have learned over their years of practice.

And on the testability question, they tested it, Special Master, they got a different result and if Ms. Martines claims that she is unaware of what numbers that Dr. Palese put in, well, I don't know what more to give her except for her sworn testimony, which she said she put in 44. Now, if Ms. Martines thinks that that is not credible, then that is absolutely a jury issue and something that is for a jury to decide whether or not they believe Dr. Palese, but Dr. Palese testified under oath as to what she put into that calculation.

THE SPECIAL MASTER: Okay. Thank you.

So I think the next one that's -- that I have on my list is Lamsita, L-a-m-s-i-t-a.

And, Tracy, are you going to be arguing that?

MS. FINKEN: Yes. Good afternoon, Special Master Reisman. It is Tracy Finken from Anapol Weiss on behalf of plaintiffs.

THE SPECIAL MASTER: Okay. Go ahead.

MS. FINKEN: Okay. As far as Dr. Lamsita's testimony goes, there are three specific opinions that

plaintiffs seek to exclude, and I'm going to go through them briefly because there has been some concessions that have been made on behalf of AstraZeneca so I just want to make it very clear on what's been conceded and versus what we are still seeking to exclude.

You are muted. Sorry.

THE SPECIAL MASTER: I said that's helpful. Sorry. Go ahead.

MS. FINKEN: So I'll just go through the three one by one.

The very first opinion that we were talking about relates to the findings of chronic progressive nephropathy in the animal studies. And AstraZeneca has conceded that Dr. Lamsita will not offer an opinion on the pathological criteria of chronic progressive nephropathy in the animal studies or the significance of chronic progressive nephropathy in rats to humans.

However, plaintiffs seek to exclude any opinion by Dr. Lamsita as it relates to chronic progressive nephropathy because by Dr. Lamsita's own admission she is not qualified to offer such opinions. She has testified that she is not an expert in kidney

function and not an expert in kidney function across species. She has testified that she is not a pathologist and she doesn't feel qualified to speak to the details around the pathology relating to chronic progressive nephropathy. That's on Page 109 of her deposition.

She has testified that she is not comfortable describing any of the inflammatory components involved in chronic progressive nephropathy in rats, and that's on Page 109.

She hasn't looked at any of the findings under a microscope. She admits that she doesn't know whether her own description of kidney findings in certain studies of nephrocalcinosis are similar to other types of kidney injuries.

She opines, though, she doesn't just regurgitate the findings in the animal study reports that AstraZeneca created, she takes it one step further. So she finds that there's are nephrocalcinosis in some of the short-term rat studies but then she takes it one step further and opines that that's an early precursor of chronic progressive nephropathy. And she has already testified multiple times that she is not qualified to give that opinion.

She also attempts to explain away the findings of a dose-dependent increase in chronic progressive nephropathy in the treated animal groups, and that's on Page 117. But because she is not qualified admittedly to discuss the pathological findings of chronic progressive nephropathy and did not actually do that, she should not be able to testify as to the cause of those kidney findings in the underlying clinical -- or preclinical animal study reports.

Dr. Lamsita says that she relies on the expert opinion of Dr. Sandusky. However, the Third Circuit law is pretty clear that for an expert to rely on the opinion of another expert, they need to be able to assess the validity of those opinions and Dr. Lamsita could not assess the validity of the opinions of Dr. Sandusky because she is not qualified to do so and she admits that.

Because she did not assess the validity of Dr. Sandusky's opinions, it renders her methodologies unreliable in accordance with Third Circuit law and you can look at the citation in our papers to In Re TMI litigation which supports that.

The second opinion that plaintiffs seek to

exclude in terms of Dr. Lamsita is that she is not qualified to give opinions about the cost of drug development generally. AstraZeneca concedes that Lamsita will not testify on the cost of the development of Prilosec and Nexium or PPIs, but they oppose our motion to exclude her testimony as to the cost of drug development generally.

And first, as it goes towards drug development, putting the qualifications aside, defendants have not provided any evidence that Dr. Lamsita is qualified to give that opinion based upon the preclinical work and experiences that she has done. There is no evidence that she has done drug development soup to nuts to give that type of opinion.

She admits that she could not provide an opinion on the cost of drug development a long time ago at the time that Nexium and Prilosec were developed, and that's on Page 85 of her deposition, but she says that she may, may be able to offer an opinion on the cost of drug development today. That's also on Page 85.

So putting aside her qualifications to give the opinion of the cost of drug development today based upon a single trade publication article, it's

critical to recognize as a practical matter that the cost of drug development today is not relevant to any issue in this case whatsoever.

So besides the lack of qualifications, there is a lack of fit. And her opinion on this issue as to the cost of drug development today should be excluded.

And then just going to the third point, and that's about Dr. Lamsita's testimony as to whether Nexium or Prilosec will be approved by the FDA today, defendants concede that -- that Dr. Lamsita would not offer an opinion on whether Nexium or Prilosec would be approved by the FDA today but only offer an opinion as to whether the nonclinical studies would likely result in approval today. That's directly from their brief at Page 36.

And this is misleading for a couple of reasons. One, Dr. Lamsita admits that when you seek approval for a drug and drug development, I think everybody on this call would probably concede this, that there are multiple factors that the FDA considers in approving a drug, only one of which is preclinical studies. The clinical studies in humans, you know, Phase 1 through 4 studies are all highly relevant to

that inquiry. And Dr. Lamsita has testified on Page 144 of her deposition that the clinical studies are a really bigger part of the drug approval process than the preclinical studies. And then she says that she didn't review the clinical studies in this case and she can't offer an opinion about the clinical data.

So any opinion by Dr. Lamsita regarding whether these drugs would or would not be approved today based on preclinical studies is misleading to the jury.

THE SPECIAL MASTER: Would you agree that she could give opinions about the adequacy of the preclinical studies for FDA consideration? I guess what I'm saying is maybe even if she couldn't go to the ultimate decision, Oh, yes, it would have been approved, it seems like with her qualifications, could she not say I've looked at these preclinical studies and at least that portion of it would be fine -- found adequate?

MS. FINKEN: I think that there are opinions that Dr. Lamsita gives in her report that are appropriate for her area of expertise that we can cross-examine her at trial on relating to, you know,

good laboratory practices and things of that nature, the process generally of submitting preclinical studies to the FDA, you know, whether or not these -- these clinical studies complied with the laboratory practices or not.

But Dr. Lamsita should not be able to testify that the drugs would be approved based upon the preclinical studies that she reviewed because the FDA can't approve a drug based on preclinical studies. They would not, they could not, they cannot do it. They have to evaluate the entire package, including the clinical studies which Dr. Lamsita has not evaluated and she has admitted as much during her deposition. And that's on Page 144 of her deposition testimony.

And with that, Special Master Reisman, I will -- I will turn over the floor to Ms. Althoff and save any other time for rebuttal. Thank you.

THE SPECIAL MASTER: Thanks.

Hi, Katherine.

MS. ALTHOFF: Hi, Special Master. Yes, I'm going to respond on Dr. Lamsita.

Again, Katherine Althoff on behalf of AstraZeneca. I'm going to take these in reverse order

because I think it goes from the simplest to perhaps the most complex issue.

Dr. Lamsita said in her deposition, I'm not testifying regarding any clinical data. Dr. Lamsita is a toxicologist. She has years of experience at FDA, in industry, and consulting, in which she worked on helping companies get their drugs approved to put on the market. She only works with animal studies. This is what she does.

And taken into context, that's exactly what she is saying here is that the nonclinical studies would have been sufficient to have these drugs approved, not that everything, the entire package would have been approved, but purely that the nonclinical program was sufficient and appropriate. So I think we agree on that, so I'm not sure --

THE SPECIAL MASTER: I'm going to make a bold statement, I think you are kind of in agreement on that.

MS. ALTHOFF: Yeah, I think so too, and so I'm not sure why, based on your our agreement, that we are having this argument today. But in any event, I think she can testify to the level that she wants to testify to on that issue.

Secondly, with regard to the drug development costs, I think this one is also pretty simple. Again, Dr. Lamsita, this is what she has done throughout her entire experience is work as part of a team in helping to get drugs approved. She said she had not reviewed any documents that specifically addressed how much Omeprazole costs to get to market nor how much Esomeprazole, that being Prilosec and Nexium, costs to get to market, and so she has no intention of testifying as to those precise numbers.

But in terms of a general opinion, if asked, about how long does it take to get a drug to market and what does it cost, I think, you know, based on her years of experience on a variety of compounds, she has got the qualifications and the expertise and background knowledge to testify to that.

THE SPECIAL MASTER: Can I ask you a question about that?

I mean, she is a toxicologist, right? I mean, how -- I'm -- how does she know what it costs? I mean, she is not like in the finance group, has she worked for companies? I mean, how does she get that knowledge? And I think she was a toxicologist at FDA, right?

MS. ALTHOFF: Yes. She was a toxicologist at FDA for a few years, she has also worked in industry and she has also worked as a consultant. And so she is part of a team. She understands how long it takes and generally what it costs.

Again, this is -- she is not going to come in as some kind of an economist or something like that, but I think at the level in which she would be asked and at the level that she discusses it in her report, I think she is qualified and got the experience and background knowledge to testify to that.

THE SPECIAL MASTER: All right. And so the remaining thing I think is the CPN?

MS. ALTHOFF: Yes, chronic progressive nephropathy. Again, I think to some extent we are talking past each other, and as I think you mentioned in one of the arguments earlier today. She is a toxicologist, she is not a pathologist, and so when she would work at FDA, she would review pathology reports, as she did in this case, she would review nonclinical study reports, as she did in this case, and if she had a specific question about the pathology, she would go talk to one of the FDA

pathologists.

That's not really what she is doing here. I mean, she is reviewing the study report, she sees what's reported, she has familiarity, as she testified in her deposition, I think it was Page 176, that from her work at FDA she is familiar with chronic progressive nephropathy, not as pathological criterion, as we've conceded she is not going to testify to, but to the determination that that's in fact something that happens in rodents, she is aware of it and she has seen it before.

And so I think to the extent she is testifying about chronic progressive nephropathy, she doesn't plan to step on top of Dr. Sandusky who is an animal pathologist. She is going to testify with regard to what was seen and to the extent that AstraZeneca provided that information to the FDA. Again, I think we are talking past each other here.

THE SPECIAL MASTER: Tracy, do you want to respond?

MS. FINKEN: If I could, please, just very briefly.

Dr. Lamsita does not just regurgitate what the animal clinical study reports say about chronic

progressive neuropathy. That's not what she does. She does that. But she also takes it one step further and she attributes what the cause is of certain kidney findings in the animal studies. While admitting in the same breath that she's -- while she has heard of CPN, or chronic progressive nephropathy, she is not qualified to opine about it but yet that's exactly what she does in her report.

And you can see that on Page 114 to 115 of her report and 117 of her report where she talks about different kidney findings that she observed in some of the animal studies and this then she opines that those are evidence of early precursors of chronic progressive nephropathy, or CPN, which is the -- a pathological finding.

And yet she admits throughout her deposition that she is not qualified to evaluate the pathological findings of chronic progressive nephropathy nor did she evaluate them and she is not comfortable giving opinions about that. But that's -- you know, what she says in her deposition and what she actually does in her report in terms of making those leaps of just not regurgitating what's in the study reports but actually attributing cause to certain

findings are two different things, and she is -- she is simply not qualified to be able to give those types of opinions.

So plaintiffs seek to exclude any testimony by Dr. Lamsita about chronic progressive nephropathy because by her own admission she is not qualified to address that.

MS. ALTHOFF: May I speak just very briefly, Special Master?

THE SPECIAL MASTER: Go ahead.

MS. ALTHOFF: The problem with that is they don't disagree that she is qualified to analyze the reports and determine the adequacy of the preclinical study program. And in the preclinical study program AstraZeneca's own investigators identified chronic progressive nephropathy. So you leave us in a strange position if you say she can't utter the words "chronic progressive nephropathy" because it's in the study reports and she is familiar with it, she is familiar with that condition from having worked at -- at FDA, and if she had questions about it there, she would do the same thing that she did here, which is talk to a pathologist.

THE SPECIAL MASTER: Okay. Thank you.

MS. FINKEN: Can I just make one point, Special Master, in response to that?

THE SPECIAL MASTER: Oh, sure.

MS. FINKEN: She is not familiar with chronic progressive nephropathy. She says she has heard of chronic progressive nephropathy. That's a big difference and that's what she states in her deposition testimony. And hearing of chronic progressive nephropathy does not render you qualified to be able to evaluate findings of kidney toxicity and determine that they are chronic progressive nephropathy or attributed to chronic progressive nephropathy, and that's exactly what Dr. Lamsita attempts to do in her report if you look at it critically. Thank you.

THE SPECIAL MASTER: Okay. Thank you both.

Okay. So the last one that we have is Andrea Leonard-Segal, an FDA expert. I believe that this -- this expert is just as to Takeda. Am I correct about that?

MS. MARTINES: That's correct, Special Master.

THE SPECIAL MASTER: Okay.

MS. MARTINES: Actually, I have kind of a dual motion. There is a motion to disqualify and then

there is one to limit her testimony.

THE SPECIAL MASTER: Yeah, I'd like to take up the motion to disqualify first, if we can.

MS. MARTINES: Of course.

THE SPECIAL MASTER: Okay. Let's do that.

Can you identify yourself?

MS. MARTINES: Okay. Yes, ma'am. Buffy Martines on behalf of plaintiffs on their motion to disqualify Dr. Andrea Leonard-Segal.

Special Master, to make a long story short on this one, in the interests of time, I know you've read all of the papers, the fundamental issue is that this expert was a long-time employee of the FDA who now purports to be an expert on the very matters that she worked on at the FDA. And under Federal law that is prohibited under the code section that we have cited, and I believe it's 18 USC 207.

THE SPECIAL MASTER: Buffy, can I stop you there for a minute?

MS. MARTINES: Of course.

THE SPECIAL MASTER: That's a criminal statute, correct?

MS. MARTINES: Yes, ma'am.

THE SPECIAL MASTER: And I guess the question,

the fundamental question that I had when I was reading through all of these materials is where is the authority to use that statute to exclude an expert in a civil case? In other words, I mean, they might be running afoul of a criminal statute by testifying and not something most people would want to do, but where do you get the authority from that statute that you can exclude in evidence -- disqualify an expert from a civil case?

MS. MARTINES: I believe the case that we cite you to is US v. Coleman, which is a Third Circuit case from 1986, 805 F.2d 474. And in that case they talk about the fact that these revisions, these provisions and then revisions to the provisions that Congress made are used in order to vent even the appearance of impropriety in these types of matters, that a former public official cannot use their position for private gain, personal or private gain. And then we also cite a couple of other cases within that same section of our brief.

THE SPECIAL MASTER: Yeah. We looked at them. I guess I didn't think, and I'll go back and look again after we have this argument, I didn't think any of them were exactly right on point here, and maybe

this is sort of a first impression issue. I don't know.

MS. MARTINES: And that could be. There is a grouping of cases that we cite that go to this. And I don't know if they are -- you know, if they are just absolutely on point, but they certainly go to the proposition that this statute -- in this statute Congress forbids the exact kind of testimony that's going to happen here or that's anticipated.

Dr. Leonard-Segal, as I said, from 2002 to 2013 worked for the FDA and was involved in -- with PPIs, including the FDA's approval of Prilosec OTC, of the OTC version of Prevacid, she oversaw labeling, adequacy of the warnings, label changes, on each product she considered renal failure as a risk, she reviewed the safety and efficacy of those products, she considered the adverse events, and she gave opinions on all of those matters with regard to both Prilosec OTC and the Prevacid OTC version.

She also oversaw the Prevacid switch from Rx to OTC versions. She discussed efficacy and safety on that product as well, part of the labeling.

Importantly, with regard to Prevacid, which is the product we are talking about here, during

her testimony in her deposition, she discussed the fact that as part of the Prevacid switch she did a comprehensive -- the FDA did a comprehensive review of all safety data and that that included Prevacid and, in fact, all of the PPIs. So she was involved -- I know that there is going to be an argument that, Oh, she was just involved on the OTC side and that makes it a lot different. I'm going to talk to you about why OTCs aren't different, which is a whole another issue, but the fact of the matter is that during the course of this work she did review Rx information, she did review safety and efficacy labeling issues, adverse event reports, and those were comprehensive reviews. And that is the very specific subject matter that she is it going to try to talk about in this litigation and that is the specific type of testimony that the statutes preclude.

THE SPECIAL MASTER: Have you made any effort to contact FDA or the Department of Justice or anybody and see if they are complaining about this?

MS. MARTINES: I have not done that personally, and I would -- I do not -- I am not aware that the USC has done that either.

Again -- oh, go ahead.

THE SPECIAL MASTER: Well, because as I read the statute and some of the cases, they are the ones who have the gripe about this, right, if she is out there, you know, doing -- engaging in this conduct, aren't they the ones who really have standing to complain?

MS. MARTINES: Well, I think they certainly -- I mean, obviously they certainly have standing to complain. I think plaintiffs also have the same issue, because part of the reason why, and the cases talk about this, the reason why this statute exists is to limit this kind of revolving door concept from governmental work to making your living off of kind of the fruits of your labor, so to speak.

The plaintiffs' issue is going to be that Dr. Leonard-Segal is going to come in, and this is included in our Daubert motion as well, she is going to come in and say, I was part of the FDA, I looked at this stuff, this is what the FDA decided, everything is great, fine and wonderful, let's go drink coffee. And that is the exact type of testimony that this -- these code sections and the cases talk about is improper. And it leaves the jury with the opinion that it is almost the FDA that's in there saying it because this woman, this doctor has been doing this

all of this time and she is going to rely on her experiences in the FDA. And the supposition, what the jury is going to be left with is, Oh, well, the FDA is in here telling us that everything is fine.

And in our Daubert motion we discuss the fact that she is relying strictly on what the FDA says about this drug. She hasn't done any of her own work on it. She is just going with all of that. And that's the exact kind of testimony that -- that the code sections and the cases discuss is improper.

The other item I would want to pick up, and then I'll reserve the rest of my time for rebuttal, is in Takeda's briefing they discuss the fact that Takeda is off the hook, so to speak, because it was actually Novartis that was applying for all of these -- for the OTC version of Prevacid and those types of things, and I just want to remind the Special Master that the code sections and the cases discuss that it doesn't have to be the exact party that -- that it's -- there is no identity of parties necessary. This isn't some kind of gotcha regulation where if you can sneak by because it is a different name, you are okay.

The fact of the matter is that when the

applications for the Prevacid OTC products were being put in, yes, Novartis was the representative on behalf Takeda and Takeda was actually listed as the supplier and manufacturer. So there is no escaping this issue simply by saying, Well, we weren't the ones that specifically were involved with Prevacid OTC application. They were certainly involved, and the statute defines them as any other person that was participating. So that is not a means of escape, so to speak.

And with that, I will reserve the rest of my time for rebuttal.

THE SPECIAL MASTER: Okay. Thanks, Buffy.

Hi, Mike.

MR. RUTTINGER: Good afternoon again. Just for the record, this is Mike Ruttinger on behalf of Takeda.

Just to clarify, are we going to argue the Daubert issues separate to Dr. Leonard-Segal following this or do you want me to address those as well?

THE SPECIAL MASTER: I think we are going to argue them separately. I don't think -- Buffy, I don't think you argued all of your Daubert issues, did you?

MS. MARTINES: I did not. I think it is a very short argument on Daubert, but we can certainly separate them up.

THE SPECIAL MASTER: Let's do it separate.

MR. RUTTINGER: Perfect.

So focusing on the disqualification issues, Special Master, you hit the nail on the head here. This is a really unprecedented argument for plaintiff to make, to request a disqualifying Takeda's regulatory expert based on an assertion that she has committed a crime when it is undisputed that there has been no charge or pending proceedings or even a request by plaintiff to the FDA to look into this.

If you look at the cases plaintiff cites, there are some that come up in the context of a motion to permit expert testimony under the exception that's built into the statute when the regulation applies, but we think that this case is a different one because the regulation, Section 207(a)(1) doesn't apply in the first place. So plaintiff hasn't identified any other case quite like this one where a court has disqualified a former FDA expert from testifying just based on her experience regulating what we believe are different drug products.

THE SPECIAL MASTER: Okay. Can I stop you for a minute there.

MR. RUTTINGER: Of course.

THE SPECIAL MASTER: You say that it doesn't apply, and I think you are going to talk about why you think that, right, but if it did apply, you would have to -- she would have to go seek permission under that regulation, correct, from FDA or from the court?

MR. RUTTINGER: Correct. The regulation exception built into the statute specifies that if those initial three criteria that are required for a finding disqualification under the statute apply, then there is an obligation to affirmatively seek permission from the court to testify.

THE SPECIAL MASTER: Yeah, from the court, you are right. And to be clear, you have not done that, right?

MR. RUTTINGER: That is correct, yes.

THE SPECIAL MASTER: She has not done that, okay.

MR. RUTTINGER: Now, we don't think that you need to get into the question of whether or not this statute can apply to disqualification when raised by a plaintiff, in the first place, because, as I've

alluded to, we don't think that plaintiff has identified that they can prevail under any of these three requirements for the statute to apply. And to be clear, the statute requires proof as to -- or I suppose to persuade the court that it applies as to all three of those elements.

So I do want to address one item quickly from plaintiffs' briefs that I believe to be a misrepresentation before we get into those three elements, and that's this repetition in both their motion and their reply brief that Dr. Leonard-Segal admitted she couldn't represent Takeda before the FDA.

If you actually look at her testimony, and it is even quoted in plaintiffs' brief, she says she couldn't represent Takeda before the FDA on the same matter on which she worked at the FDA. As I go through those elements, one of which is the particular matter requirement, I think you'll understand our position as to why we don't believe that her testimony there is at all inconsistent with the statute because it is not the same particular matter.

THE SPECIAL MASTER: This is the argument that she worked on OTC, not on -- not on prescription?

MR. RUTTINGER: In part, yes, that's correct.

So I think it makes sense to start with that particular matter issue, and so the first requirement under the statute is that, you know, the United States must be a party or have a direct and substantial interest in the particular matter at issue.

Well, the United States was not a party, so let's think about what does direct and substantial interest in a particular matter at issue mean. And there are two components to that, right. So the regulations here interpreting the Ethics in Government Act, the 2641.201, it confirms the United States is neither party to nor does it have any direct and substantial interest in a particular matter, merely because a Federal statute is at issue or the Federal Court is serving as a forum for resolution of the matter.

So our position is that the United States doesn't have a direct and substantial interest for purposes of this statute just by virtue of the fact that this is litigation involving, you know, failure to warn claims, particularly when it's brought by a private entity and not by a governmental entity.

It's also worth noting, I think, and

Special Master, you raise this question of, you know, what's sort of enforcement provision for the Ethics in Government Act. Well, that regulation, 2641.201(j)(2), actually sets for a procedure for an agency to follow when it is unclear whether or not the agency has a direct and substantial interest in a matter. And it states forth a process by which there is actually a government procedure and a little bit of a hearing process to determine is this an issue in which the government has a direct and substantial interest.

So the fact that there is no pending proceeding here suggests to me that that first element, the direct and substantial interest test, can't be satisfied.

THE SPECIAL MASTER: Hold on. Who would be bringing such a procedure? The FDA, right?

MR. RUTTINGER: So it could also be brought by -- actually, if you'll bear with me for a moment, 2046 -- 2641.201(j) specifies that the proceeding must be brought by, one moment here, coordination by designated agency ethics officials.

So the ethics department has designated ethics officials for the former employees's agency, so

the FDA has these officials, who have the primary responsibility for coordinating the determination of whether a substantial interest is at issue. So it would be brought by the FDA counsel.

THE SPECIAL MASTER: Yeah, stop for a moment. So they would have to know that she was intending to give such testimony, right, and then decide if they were going to do anything about it. And I guess the question I have for you is, you know, has she made the FDA aware that -- that this is something she is going to be doing or wants to be doing?

MR. RUTTINGER: The record isn't clear on whether there has been any correspondence with the FDA, as far as I am aware, Special Master. The regulations themselves are also silent as to what the obligation is to provide notice to the FDA or any agency and how that information is followed up upon.

THE SPECIAL MASTER: Yeah, but, I mean, I guess just as a practical matter, how are they supposed to know about it?

MR. RUTTINGER: Right. And the regulations are silent on this, I think probably because this is, as you noted, something of an unprecedented issue.

Now, this is also wrapped up in the particular matter issue, though, and here is why I don't think this has to be resolved on just the direct and substantial interest. When you look at the same regulations for how to define a particular matter, particularly this is Paragraph (h)(2) to that regulation, the FDA provides -- or sorry -- the Ethics in Government Act regulations provide an example that we think is quite applicable to this situation. And the example they provide is one in which a former government official while working at the FDA was involved in promulgation of a rule applicable to a category of a particular type of medical device made by multiple manufacturers. And the example goes on to say, If the regulation was not limited in application to the particular companies already existing but it is, for example, open-ended, it would not be a particular matter involving specific parties.

So an issue of a former FDA official having spent time at the FDA regulating an open-ended class of a drug or medical device does not arise to the level of particularity required by the act to be a particular matter on which the government has a direct or substantial interest.

So we think that under either prong, under either category of that first prong of the test, plaintiff cannot show that it is applicable.

There is also the second category, and the second prong of the test is the OTC issue that plaintiffs counsel alluded to. And essentially their argument is premised on Dr. Leonard-Segal's involvement in the over-the-counter switch of Prevacid 24-hour. And plaintiff has taken the position in their briefs that because Prevacid 24-hour involves the same active ingredient as prescription Prevacid it is functionally the same matter.

And you heard Ms. Martines refer to Dr. Leonard-Segal as having worked on the same labeling and same issues as she's opining on in this litigation. That is just unfortunately not true and it, I think, it shows a misunderstanding of the Durham-Humphrey Act under which over-the-counter drugs are regulated.

So under the Act, the FDA actually requires for an over-the-counter drug to be marketed that there be meaningful differences within a regulatory sense, "meaningful difference" is a term of art in this context, from prescription drugs. In the

case of Prevacid 24-hour versus prescription Prevacid, that includes different indications for use. Prescription Prevacid has I believe ten different indications for use versus just a couple for Prevacid 24-hour, different patient populations, different labeling, and fundamentally different NDA numbers. So they are, within all respects regulated by the FDA, different drug products.

So Dr. Leonard-Segal's involvement with prescription Prevacid is simply not the same prescription drug product or not the same drug product at all that she is testifying on in this litigation.

As to the third criteria involving specific party or parties, it is not our position, as Ms. Martines suggested, that the parties have to be identical for purposes of whether or not the statute applies. The fundamental issue here, and if you look at the cases cited on Page 20 of plaintiffs' motion to disqualify where they talk about cases of limited expert testimony and other testimony in these cases, all of these cases talk to the fundamental concern underlying the statute of side switching. It is the idea that former FDA official or a former government official of any kind has left government employment

and is switching sides and offering testimony against the government or against the government's interests on the exact same issue. When the government isn't a party here, isn't involved in private failure to warn litigation and the work that she did is on a different drug product than is at issue in this case, different warnings and different labels than are at issue in this case, the whole side switching burden simply isn't met here.

So as a result, we don't think that either the first, second or third criteria of the Ethics in Government Act are satisfied here, and if even one of those doesn't favor disqualification of Dr. Leonard-Segal, then plaintiffs' motion should be denied as a whole. They have to prevail on all three of those prongs of the statute to even argue that disqualification can occur, assuming in the first place that this court can use a criminal Ethics in Government Act statute as a basis for excluding expert testimony.

THE SPECIAL MASTER: So a couple of other questions.

I mean, if -- if she -- if we said okay, she can testify, does that expose the court, this

process to any kind of risk? I mean, should the court seek FDA approval, input on the question here?

MR. RUTTINGER: I don't -- I believe the answer to that is no, Special Master. The statute itself, assuming that there -- the application of these three provisions is kind of a mixed question of fact and law, right. So the court's determination of that will, you know, in any potential appeal or something of that issue, be subject to the same kind of standards where it will be a, you know, an abuse of discretion standard as to whether disqualification is appropriate and a de novo standard as to any of the legal issues underlying that. But there is no, you know, sanction for the court in determining this. It should be ultimately decided under the same discretionary standard for admission of evidence that would normally apply with the application of the ethics in government issue being a legal issue that the reviewing court would need to decide.

THE SPECIAL MASTER: And I guess I might have asked this before, but maybe not clearly, I mean, are you aware of whether she has ever raised this with the FDA?

MR. RUTTINGER: I am not aware of that based on

the record that I have seen, but I can't speak conclusively to that.

THE SPECIAL MASTER: Okay. All right. Because, I mean, in some respects, you know, if you were right about all of this, then what's the harm in going to FDA and, you know, saying this is what I'm doing, I just want to make sure you're okay with it?

MR. RUTTINGER: I guess I would say, in response to that, that the harm it could extend is, it is not unique to this case, it is that what plaintiff is really suggesting here is, you know, an unnecessary procedural obligation that doesn't have a basis in law that could really quickly roll out of control.

A lot of the issues that Ms. Martines identified as her concern for this, this notion of a revolving door between the FDA and the government and an expert stepping in, saying, Well, I worked at the FDA and here is what the FDA would say about that, I'm not sure I understand how that's really different from someone like Dr. Ross coming in and offering testimony when he is going to say I'm talking on my basis of a -- on the basis of my experience at the FDA and the imprimatur that brings.

Now we are not arguing that Dr. Ross is

disqualified under the statute. We don't believe it applies here and we don't believe it applies there. But you can quickly see how this might get out of control.

THE SPECIAL MASTER: Yeah, but I think the question is, here, is you say OTC and prescription are very different matters. And Ms. Martines says, no, they are not. You know, they are certainly a whole lot closer than what most FDA experts that I've seen over the years are willing to testify about based on their experience. So, I mean, I think -- you know, I think that's the difference. That's why it doesn't apply to Dr. Ross or Dr. Mann. I think it's -- you know, you've got an expert here who undoubtedly was involved with the OTC products and their labeling and their adverse event review at FDA and I guess the question is, as you've already discussed, you don't think it is the same particular matter, but, you know, I can see why someone would raise that question certainly.

Anyway, Buffy -- or Mike, do you want to add anything else?

MR. RUTTINGER: Oh, I was just going to add a single sentence there, which was, you know, I think

the similarities are misleading in this case because ultimately this case boils down to labeling, right. It boils down to failure to warn claims, at least in the Bales case which is the only one in which Dr. Leonard-Segal is being disclosed as an expert, and the labeling issues between a prescription drug and over-the-counter drug are fundamentally different because they are different labels and different products.

So I think that the dissimilarities here are more pronounced when this court looks at the labeling issue and that they are labels for different products. That's all I have.

THE SPECIAL MASTER: Okay. Thanks, Mike.

Buffy, did you want to follow up?

MS. MARTINES: Yes, please. Let's start with switching sides, Item No. 1.

Dr. Leonard-Segal is absolutely switching sides. Her work at the FDA was on behalf of the government, and as everyone on this call knows, the process of getting a drug approved with the FDA is inherently an adversarial process with the manufacturer. There are negotiations, there are discussions, there are all kinds of things. During

that process, while she worked there, she worked for the government and she represented the FDA.

And she represented the FDA on a lot of issues. One -- a couple of things I forgot -- I neglected to mention. The 2011 citizens petition, a very important issue, and the 2012 tracked safety issue regarding PPI-induced AIN. Dr. Leonard-Segal testified that she more than likely would have been involved in both of those issues, which are class-wide issues. She would have worked for the government during that time on behalf of the FDA in opposition of the manufacturers.

So now she has left the FDA, she has switched sides, she is working for the manufacturers now in a United States District Court. She testified that she wouldn't be able to be in front of the FDA representing Takeda. She cannot go in front of the United States District Court either. The government is a single entity. We've cited that in our brief. The government is a single entity, whether it is the FDA or the court, she can't do it. She cannot switch sides, which is exactly what she is trying to do.

Now let's talk about OTCs. You just heard the party line on prescription versus OTCs when it

suits the manufacturer, and this is an issue that I have gotten into very deeply. You'll hear more about it in the next round of cases, but these manufacturers have a history, a history of marketing these drugs, whether it's a prescription drug or an OTC, however they want. They are interchangeable when they are marketing them or when they are trying to steal somebody else's market share. When studies come out that say there is something wrong with PPIs, all of a sudden it is a big -- whole different issue, OTCs and prescriptions are completely different. When they want to bring an expert to court who has worked on this product who shouldn't be there, oh, all of a sudden OTCs are different than prescription. It is a distinction without a difference. We are talking about the same type of warnings, we are talking about the same injuries, we are talking about the same formulation, we are talking about the same manufacturers making money on these drugs, making money on these drugs. It is a distinction without a difference and they should not be allowed to play some kind of smoke and mirror games with whether these are the same products or not.

Dr. Leonard-Segal worked on this product,

this specific product while she was at the FDA. She worked on OTC issues, she worked on prescription drug issues, she did comprehensive evaluations, she looked at the citizens petition, she looked at the track safety issues. She is up to her neck in this specific issue and she -- under these statutes that we are citing and under the case law that we are citing, she is not allowed to do that and she should be disqualified.

Thank you.

MR. RUTTINGER: May I have a true 15 seconds?

THE SPECIAL MASTER: You may.

MR. RUTTINGER: Special Master, I'd encourage you again to look at that CFR 2641.201(h)(2), Example 5, about the former FDA official, that makes clear to me that involvement in class-wide class labeling and other types of issues is not involvement in a particular matter within the meaning of the statute.

THE SPECIAL MASTER: Okay. I will look at it.

Okay. So Daubert, did you want to -- do you have more to say about that?

MS. MARTINES: Well, just a little bit. I don't -- I don't want to belabor some of these points,

and the papers, this was a short motion on Dr. Leonard-Segal and I know that you've already taken a look at those.

Just very quickly, she has basically got two opinions, as best I can tell, that Takeda acted appropriately in its labeling and that there is no causal association between PPI use and the kidney injuries.

And I want to start by saying the doctor has already conceded that she is not qualified to speak about causation in her deposition testimony, Page 93, lines 18 and 19, she specifically says: "I don't testify as a medical -- as a medical officer expert giving my opinions about causation."

I'm not -- it's a little bit hard for me to tell in Takeda's papers, and maybe we'll get some clarification on this, I think that they concede that she is not qualified or she is not going to speak about causation, but I'll -- I won't speak for them, but she should -- she has conceded that she can't speak to causation issues, that she is not testifying as a medical officer or a doctor in that area.

So we believe at a very minimum she can only testify to regulatory issues. Now, I'm not

waiving my argument that she shouldn't be testifying at all, but for purposes of what we are talking about, at a minimum limited to regulatory issues.

THE SPECIAL MASTER: I think there was a stipulation that she is not going to offer a medical causation opinion.

MS. MARTINES: And that may very well be true. I hope so. I hope that's the case because that makes things a lot cleaner.

With regard to the opinions that she does give and her methodology and how she did that, she testified that she didn't review any underlying data, she has reviewed no published literature and that she relies strictly on the assessment or actions of the FDA and Takeda as support for her testimony.

In fact, she said in her testimony that she is not basing her review on any nephrology information and any medical evidence on anything related to kidney injuries and that she is only testifying with regard to certain regulatory items, including the label.

Now, with regard to those conclusions, the problem with those opinions I believe is that she -- they are all supported by -- only by assumptions. She

stated that -- she specifically stated in her deposition, again, at Page 119, Lines 11 through 22, that she comes to these conclusions because she assumes the FDA must have seen data or had discussions.

And you simply cannot base any kind of expert opinion on assumptions and speculation that you have no proof of. That's certainly not a reliable methodology that -- that she can bring to court under -- under the applicable Daubert standards.

So with that, I will -- I will reserve the rest of my time for rebuttal.

THE SPECIAL MASTER: Thanks, Buffy.

Mike.

MR. RUTTINGER: I will keep this very short.

So first off, to clarify, Dr. Leonard-Segal will not be offering medical causation or kind of regulatory causation opinions in this case. So that should make this all a little bit cleaner.

What she is going to offer is testimony based on her experience about what FDA did and what various interactions between the manufacturer and the FDA mean in terms of providing context for that, which

she can do as a former FDA official who has the experience of being involved in those kinds of interactions.

Now, what plaintiff has said is their main Daubert challenge here is a criticism of the fact that she didn't look at, say, some of the underlying nephrology studies and data. That's information that might be important if she was offering the kind of regulatory causation opinion that, say, Dr. Ross is offering. She is not. The opinions she is offering here, they are not based on assumptions. They are based on her experience at the FDA and having done this kind of job and having worked with the FDA and seen interactions between FDA and manufacturers and being able to tell a jury, because these are complicated issues after all, what it means when a manufacturer submits X to the FDA and what it means when the FDA reacts in such a way. We think that that's all based on her experience and qualifications which plaintiff here doesn't appear to be contesting, and we think that that's sufficient and that there are many other cases cited in our Daubert reply in which the kind of regulatory testimony that she is offering has been readily allowed under Rule 702.

THE SPECIAL MASTER: Okay. Buffy?

MS. MARTINES: Thank you very much for that clarification. We will certainly rely on that.

The problem is she is going to give an opinion that the label was inadequate and to do that she needs to base it more on what she assumes the FDA saw and what she assumes they should have discussed and what she guesses would have happened. She needs more than that if she is going to give an opinion on whether or not the label was adequate. And her testimony is that that's all she did was rely on assumptions and speculations and that's simply not enough for an expert opinion to be presented to the -- to a jury.

So with that I will conclude.

THE SPECIAL MASTER: Okay. I think we are done for today, unless I missed something. I hope I didn't. Thank you all very much, and we will resume at 10:00 a.m. tomorrow.

MR. BROWN: Ellen, one quick issue. I know we have a court reporter. This is Arthur Brown from Arnold & Porter. I'm hoping that you can circulate the rough, to the court reporter, as soon as you can. I'm happy if I need to sign anything, just to shoot it

over to my e-mail.

THE SPECIAL MASTER: Juliana, or whoever is on from Golkow, what's the process for that?

THE COURT REPORTER: I will shoot an e-mail over to him.

MR. BROWN: Thanks, Juliana.

THE SPECIAL MASTER: I'll forward -- maybe we can forward it around to everybody who wants it.

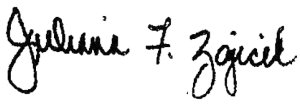
Okay. All right. Thanks everybody, very good. See you tomorrow.

Thereupon, at 3:33 p.m., on Monday, April 4, 2022, the hearing was adjourned.

CERTIFICATE OF OFFICER

I, JULIANA F. ZAJICEK, a Registered Professional Reporter, Certified Shorthand Reporter and Certified Realtime Reporter, do hereby certify that I reported in shorthand the proceedings had at the remote hearing aforesaid, and that the foregoing is a true, complete and correct transcript of the proceedings of said hearing as appears from my stenographic notes so taken and transcribed under my personal direction to the best of my ability.

IN WITNESS WHEREOF, I do hereunto set my hand on this 8th day of April, 2022.



JULIANA F. ZAJICEK, Certified Reporter